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## Solitary Pulmonary Abscess Treated by Primary Pulmonary Resection.<sup>1</sup>

By

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Copenhagen.

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Radical operation, lobectomy, and pneumonectomy are generally reserved for particularly complicated cases of pulmonary abscess, such as multiple abscesses, attending bronchiectasis, extensive pneumonitis, recurring haemoptysis, and perforation with circumscribed empyema (LINDSKOG). Solitary abscesses without these complications are usually treated by pneumonotomy, a simple broad opening. In cases of fresh abscesses having been present for up to a few months only the pneumonotomy will give favourable results; the cavity will generally close completely under suitable after-treatment.

Pulmonary abscesses of longer standing, on the other hand, are less inclined to heal after pneumonotomy. The surrounding dense fibrous tissue, due to chronic pneumonitis, granulates less readily and prevents expansion of the lung. Chronic, epithelized cavities and bronchial fistulas will often persist for years. Such cases need prolonged out-patient treatment, and the closing frequently requires secondary operations, such as thoracoplasty, muscle implantation, etc. Secondary lobectomy is in these cases a rather difficult operation, which involves a considerable risk of complications (LINDSKOG). Numerous patients never recover.

Gradually as the risk involved by lobectomy has become greatly reduced the idea has suggested itself of performing this operation primarily — prior to drainage (but, of course, after suitable, pro-

<sup>1</sup> Read before the Danish Society of Surgery on March 8, 1947.

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longed, pre-operative treatment) — in cases of pulmonary abscesses of fairly long standing, even when they are solitary and not associated with the above complications. The selection of cases suited for this operation has not yet been systematized. Our material collected so far of solitary pulmonary abscesses treated primarily by radical operation will therefore be presented in this paper as a contribution to the indications for radical operation in preference to pneumonotomy.

### Material.

Of 86 patients with putrid, solitary, pulmonary abscess seen within the period of 1944 to 1946 incl. 12 were treated primarily by radical operation (13.9 %). To these may be added 2 cases of pulmonary tuberculosis — among ab. 500 — where radical operation was performed because of severe putrid mixed infection in the cavities. The operations were as follows:

Pneumonectomy .....	2 cases
Lobectomy .....	11 cases
Segmentary lobe resection .....	1 case
Total .....	14 cases

Secondary lobectomy after pneumonotomy was not done within this period. Pneumonectomy for multiple abscesses (excepting bronchiectasis) was done three times. These cases will no more than those of bronchiectasis with attending abscess be dealt with here.

The series of cases comprises seven men and seven women. Six of the patients were under 40 years of age, five between 40 and 49, and three over 50.

One patient only (case 6) was operated on within 2 months of illness. In eleven cases (79 %) the disease had lasted for more than 6 months, and in seven (50 %) even more than 12 months. Ten of the patients had been in hospital for more than 3 months, and four of these even for more than 6 months.

All the patients presented pulmonary abscess with putrid expectoration. The maximum amount of sputum, seen in the pre-operative period, was in most of the cases (12) over 200 c.cm. within 24 hours. In five patients it was more than 400 c.cm. In two cases a maximum of nearly one litre was expectorated in the course of 24 hours. Before the operation the amount of sputum

was reduced to under 20 c.cm. in five patients, to under 50 c.cm. in three, and to under 100 c.cm. in three others. The remaining three patients had to be operated on while still expectorating from 100 to 400 c.cm. within 24 hours. The putridity had disappeared before the operation in ten patients, but persisted in four, two of whom expectorated the greatest amounts of sputum.

Three patients had intermittent profuse haemoptyses. One of them was operated on while bleeding (case 12).

The abscesses were localized as follows:

Upper lobe of right lung .....	2 cases
Middle lobe of right lung .....	1 case
Lower lobe of right lung .....	6 cases
Upper lobe of left lung .....	2 cases
Lower lobe of left lung .....	3 cases

Thus the right lung was affected in nine cases and the left in five. The site of the disease was the upper lobes in four cases, the middle lobe in one, and the lower lobes in nine cases.

The abscesses were generally rather considerable in size, measured on the removed specimens. The diameter of cavity plus thickness of the surrounding fibrosclerotic tissue was in four cases under six centimetres, while in ten cases the changes were more extensive, thus in three 10 to 12 cm.

*Predisposing diseases* were found in six or seven patients:

Tuberculosis with severe putrid mixed infection in the cavities .....	2 cases (2, 12)
Unspecific stenosing bronchitis .....	3 cases (1, 13, 14)
Bronchial asthma and sinusitis .....	1 case (3)
Actinomycosis (?) .....	1 case (7)

In the last case mentioned actinomycosis-like elements were demonstrated histologically in the removed tissue. Repeated subsequent cultivations from sputum revealed no actinomyces.

The unspecific stenosing bronchitis, which is a but little noticed, yet hardly very rare disease, has been described in greater detail by HANSEN & SMIDT (a).

In the remaining seven patients no cause of the disease could be demonstrated, except occasionally bad oral hygiene. There are found no cases of postoperative pulmonary abscesses in the present series. One patient (10) was under treatment for syphilis.

Patho-anatomical and histological examinations revealed facts that were typical for the disease in question. In no case was there associated bronchiectasis.

### Indications.

The following factors contributed in the present series to the choosing of radical operation in preference to pneumonotomy:

1. Time of existence of the abscess.
2. Recurrence.
3. Size.
4. Severe pneumonitis.
5. Intermittent profuse haemoptyses.
6. Concurrent tuberculosis.
7. Suspicion of bronchial cancer.
8. Site
  - a. under the shoulderblade.
  - b. high in the axilla.
  - c. mediastinally.
  - d. deep in interlobar fissure.
  - e. difficult to localize.

While the seven former factors indicated radical operation chiefly in cases running a chronic course, the eighth factor, *i. e.* that of site, gave rise to contemplations of radical operation already in cases of acute abscesses.

As a rule two or more of the above factors were present in the individual cases. Hence it is illusory to set up certain rules for instance as to the time of existence and size that an abscess must exceed before radical operation should be decided on.

In most of the cases the patients were admitted to the Department of Thoracic Surgery after long conservative treatment of the pulmonary abscess, sometimes because it was mistakenly diagnosed either as tuberculosis (1 and 9), recurrent pneumonia (3, 7, and 10), or inoperable bronchial cancer (14).

In other cases the patients were admitted to the Department at an early stage of the disease. Three of these (4, 5, and 11) seemed to have recovered after conservative treatment, but the abscesses recurred later and were therefore submitted to radical operation.

In some cases the abscess was localized in an area where pneumonotomy would be risky and later changing of dressing difficult, *e. g.* high up in the axilla (8 and 13), under the shoulder blade (3), in an interlobar fissure (11), or mediastinally (7 and 14). In the two latter cases (11 and 14) the localisation was doubtful before the operation. In two cases (2 and 12) there was indication for lobectomy because of tuberculosis. Bronchial cancer was suspected in two cases (1 and 14) — on account of pre-operative cytologic and histologic findings.

In one case (6) the abscess had destroyed most of the right inferior lobe. Bronchoscopy revealed an unusually broad communication between the abscess cavity and the bronchial tree. On this account the chance of a persistent bronchial fistula was regarded as particularly great after pneumonotomy, and lobectomy was therefore decided on.

### Case Histories.

*Case 1.* (162/1943.) Man, aged 54. Ill for six months, suspected of pulmonary tuberculosis. Putrid sputum, maximally 50 c.cm., pre-operatively 10 c.cm. Sputum negative for T. B., positive for tumour cells (cf. WANDALL, case 121, p. 41). Indication for operation: Suspicion of cancer, chronic course. *Left lower lobectomy* (TAGE KJÆR). No signs of tumour on palpation. Diameter of abscess 3 cm., thickness of wall 3 cm. Presumably primary stenosing unspecific bronchitis. No malignancy. Recovered.

*Case 2.* (8/1944.) Man, aged 22. Cavernous pulmonary tuberculosis. Putrid mixed infection in the cavity of 6 weeks' duration, highly feverish. Sputum putrid, maximally 500 c.cm., pre-operatively 230 c.cm., still putrid. *Left lower lobectomy* (TAGE KJÆR). Immediately afebrile and without expectoration (Fig. 1). The abscess 10 plus 4 cm. Died nine months after the operation of contralateral tuberculosis.

*Case 3.* (243/1945.) Woman, aged 48. Asthma, bronchitis, and sinusitis of 20 years' duration. Intermittent fever of one year's duration, five months in hospital. Sputum maximally 280 c.cm., pre-operatively 170 c.cm. Indication for operation: Chronic course, site of the abscess under the shoulder blade. *Left upper lobectomy* (TAGE KJÆR). Size of abscess 5 plus 2 cm. Postoperative atelectasis of left inferior lobe. Bronchoscopy. Recovered.

*Case 4.* (260/1945.) Man, aged 50. Ill for seven months, four of which in hospital. Sputum maximally 175 c.cm., pre-operatively 40 c.cm. Indication for operation: Three times recurrent intermediate lobe abscess. *Right middle lobectomy* (TAGE KJÆR). Size of abscess 2 plus 5 cm. Recovered.

*Case 5.* (28/1946.) Woman, aged 48. Ill for eighteen months, five of which in hospital. Four profuse haemoptyses. Sputum maximally 120 c.cm., pre-operatively 20 c.cm. Indication for operation: Chronic course, haemoptyses. *Right lower lobectomy* (TAGE KJÆR). Size of abscess 2 plus 5 cm. Recovered.

*Case 6.* (209/1946.) Woman, aged 28. Ill for six weeks. Sputum maximally 650 c.cm., pre-operatively 80 c.cm. Pre-operatively repeated series of direct endobronchial treatment of the abscess cavity with aspiration and injection of penicillin and alphasol (Fig. 2). In-

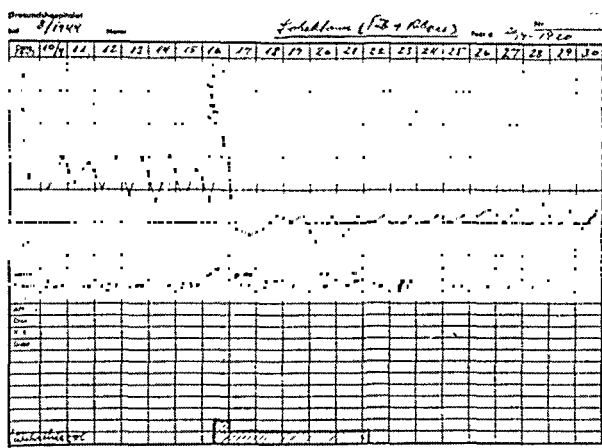


Fig. 1. Case 2. Cavernous pulmonary tuberculosis with severe putrid mixed infection and high fever. Prompt fall in temperature and cessation of expectoration after lobectomy.

dication for operation: Big abscess with very broad communication with the bronchial system. *Right lower lobectomy* (TAGE KJÆR). Possibly minor lesion of the abscess during the operation. Size of abscess 9 plus 3 cm. Bronchial fistula and empyema. Stayed 12 weeks in hospital after the operation. One year after the operation still a small bronchial fistula discharging 2 to 5 gm. within 24 hours. Feels fit and does not want to be operated on for the fistula.

*Case 7.* (213/1946.) Man, aged 33. Ill for four months. Four times in hospital within three months. Sputum always putrid, maximally 150 c.cm., pre-operatively 80 c.cm. Indication for operation: Chronic course (Fig. 3). *Left upper lobectomy* (JENS L. HANSEN). Size of abscess 4 plus 3 cm. Microscopy: Actinomycosis-like elements. Sputum after operation: No actinomyces. Postoperative atelectasis of left inferior lobe. Bronchoscopy. Otherwise uncomplicated course (Fig. 4). Recovered.

*Case 8.* (277/1946.) Man, aged 50. Ill for seven months. Sputum maximally 250 c.cm., pre-operatively 20 c.cm. After septic recurrence (Fig. 5) three weeks' stay in the country before operation. No dyspnoea. Electrocardiogram revealed nothing abnormal. General con-

dition good. Indication for operation: Chronic course with recurrence, severe pneumonitis, atelectasis, subscapular site of the abscess. *Right upper lobectomy* (TAGE KJÆR). Size of abscess 3 plus 5 cm. The operation took two hours and ran a normal course. Curare was applied for the anaesthesia. After a normal postoperative course the first

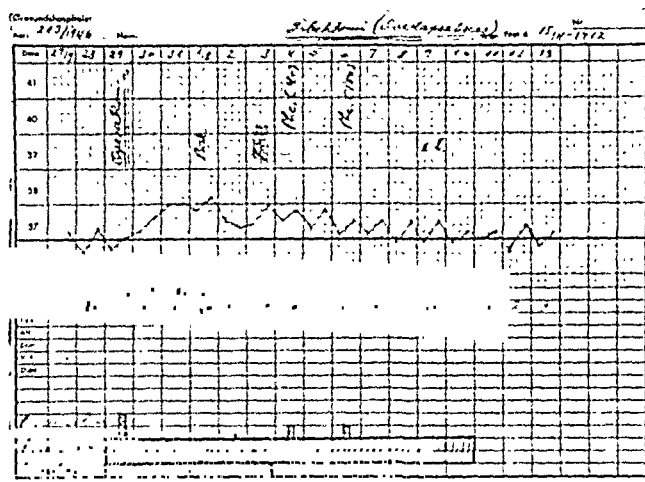


Fig. 4. Case 7. Same patient as fig. 3. Course after lobectomy.

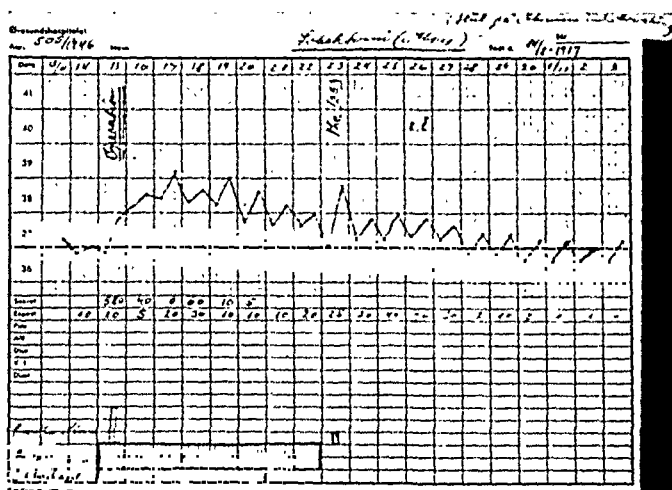


Fig. 7. Case 9. Same patient as fig. 6. Course after lobectomy, during which the abscess was injured. No empyema.

fifteen hours sudden cardiac insufficiency and death eighteen hours after the operation. Autopsy: Hypertrophy of right ventricle of the heart; otherwise nothing special (cor pulmonale).

*Case 9.* (505/1946.) Man, aged 29. Ill for seven months. Four months in hospital, three of which in tuberculosis sanatorium. Sputum negative for T. B. Several haemoptyses of up to 1000 c.cm. Maxi-



mal expectoration of sputum unknown, pre-operatively 10 c.cm. Indication for operation: Chronic course, severe pneumonitis (Fig. 6), haemoptyses. *Right lower lobectomy* (JENS L. HANSEN). The abscess was injured during the operation. Size of abscess 3 plus 5 cm. Uncomplicated course (Fig. 7). Recovered.

*Case 10.* (512/1946.) Woman, aged 32. Under treatment for syphilis of two years' duration. Ill for eighteen months, suspected of tuberculosis. Sputum negative for T. B. Sputum maximally 280 c.cm., pre-operatively 10 c.cm. Indication for operation: Chronic course, severe

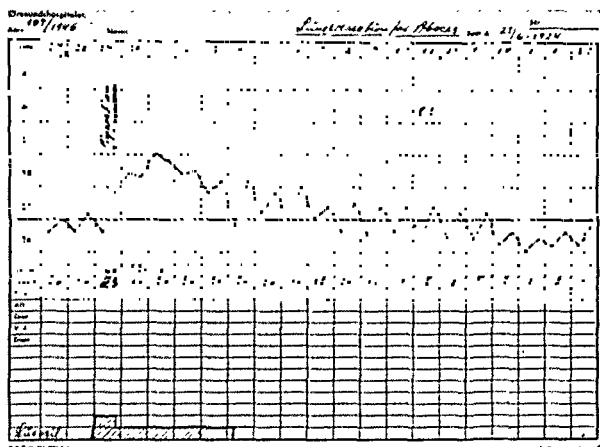


Fig. 8. Case 11. Course after resection of anterior portion of inferior lobe on account of recurrent putrid abscess.

pneumonitis. *Left lower lobectomy* (TAGE KJÆR). Size of abscess 2 plus 4 cm. Postoperative empyema. Costal resection and drainage by aspiration. The fistula closed in the course of three months. Recovered.

*Case 11.* (109/1946.) Woman, aged 21. Ill for eleven months. Three stays in the Department on account of a minor abscess, which each time seemed to respond promptly to conservative treatment. Sputum maximally 250 c.cm., pre-operatively 20 c.cm. Indication for operation: Recurrent abscess, the site of which is difficult to localize; presumably interlobar. *Resection of right lower lobe* (TAGE KJÆR). The abscess localized in the infero-anterior portion of the inferior lobe towards the interlobar fissure. Parietally to this free pleural space. Size of abscess 2 plus 2 cm. Course uneventful (Fig. 8). Recovered.

*Case 12.* (353/1946.) Woman, aged 44. Cavernous pulmonary tuberculosis with intermittent putrid mixed infection of several years' duration. Highly feverish the past three months. Repeated profuse haemoptyses. Sputum maximally 700 c.cm., pre-operatively 200 c.cm. Moreover continual haemoptyses (Fig. 9). *Right lower lobectomy* (TAGE KJÆR). Size of abscess 8 plus 2 cm. Afebrile and greatly reduced expectoration after the operation. No haemoptyses. Subsequently, cavity

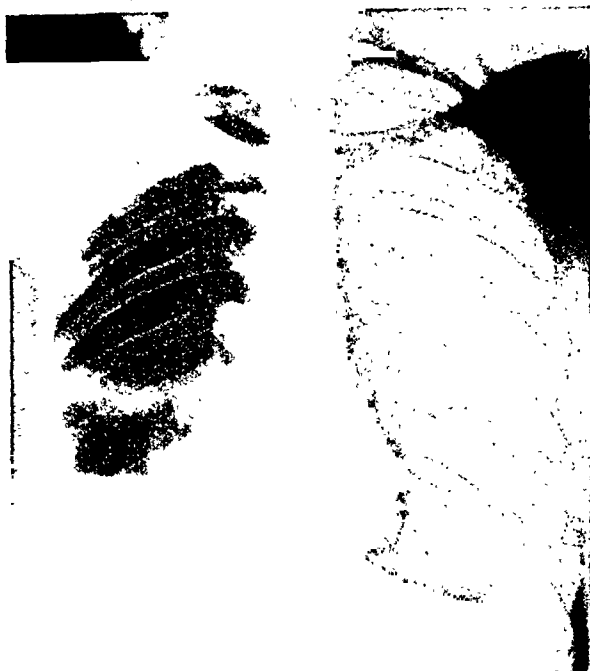


Fig. 2. Case 6. Putrid pulmonary abscess after bronchoscopic aspiration direct from the cavity.

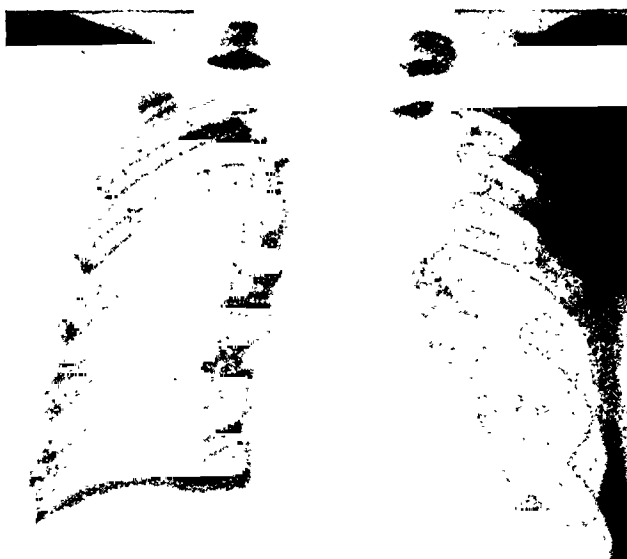


Fig. 3. Case 7. Putrid pulmonary abscess of four months' duration (actinomycosis?).



Fig. 5. Case 8. Septic recurrence of seven months old putrid pulmonary abscess. Died of cor pulmonale after lobectomy at the inactive stage.



Fig. 6. Case 9. Putrid pulmonary abscess of seven months' duration with recurrent haemoptyses.

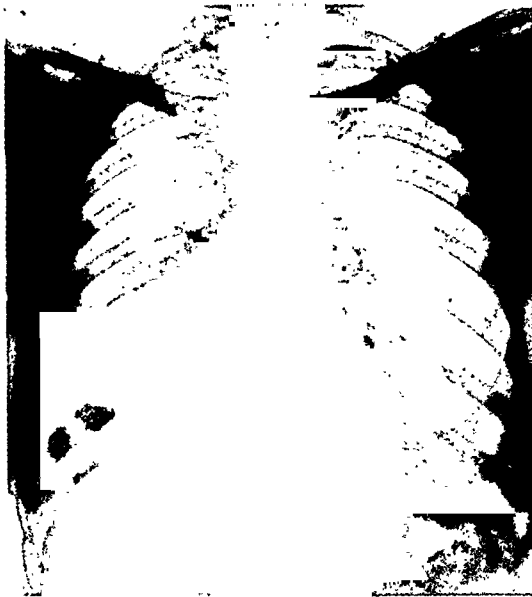
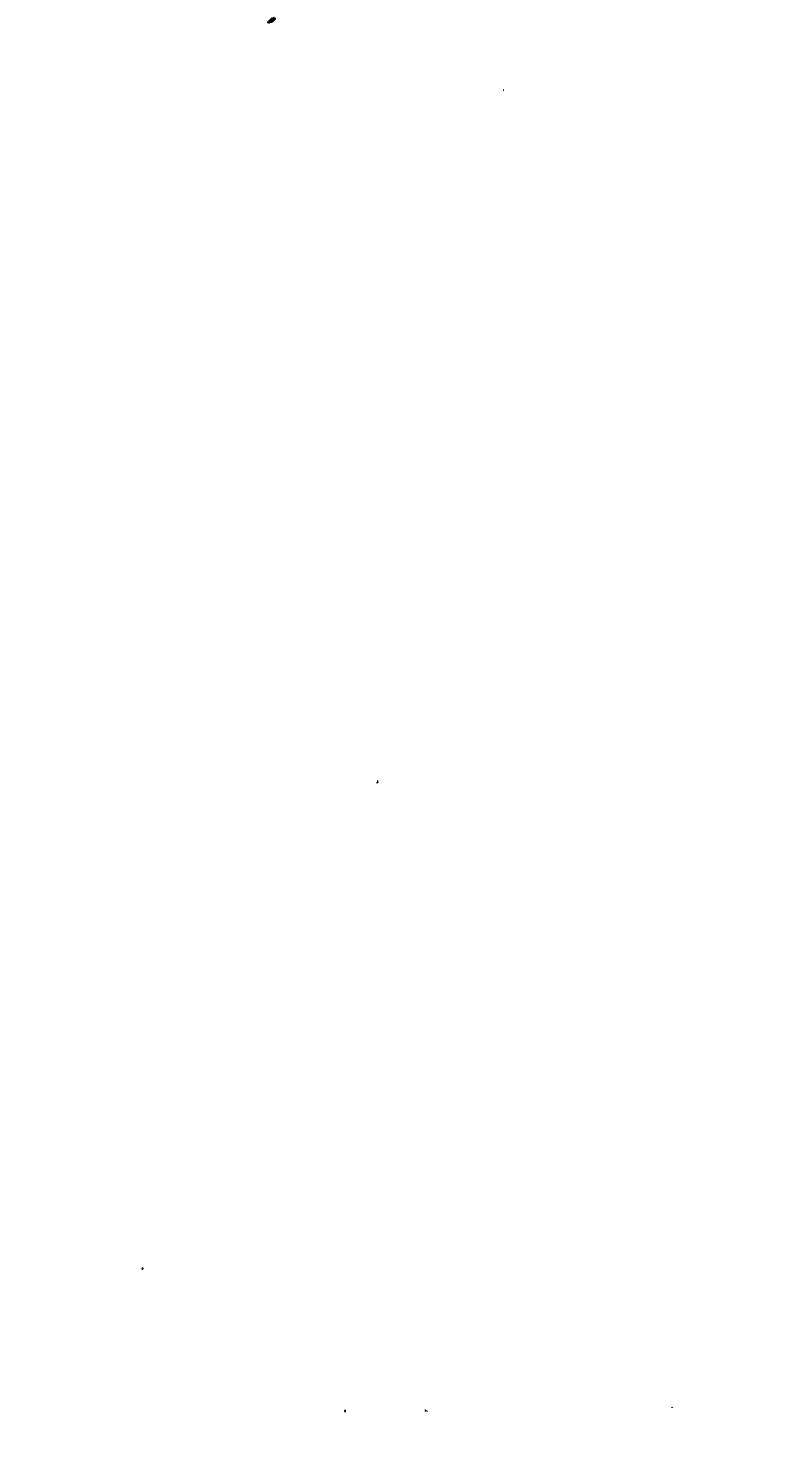


Fig. 9. Case 12. Cavernous pulmonary tuberculosis with severe putrid mixed infection and haemoptyses.



in right upper lobe. Died, one year after the lobectomy, after thoracoplasty carried out in two stages.

*Case 13.* (143/1947.) Man, aged 47. Ill for five months. Treatment with intrapleural pneumolysis was attempted but with no effect. Sputum maximally 340 c.cm., pre-operatively 80 c.cm. Indication for operation: Chronic abscess localized high in the axilla. *Right pneumonectomy* (JENS L. HANSEN). Size of abscess 5 plus 4 cm., extending to the lower lobe. Presumably primary stenosing unspecific bronchitis. Course uneventful. Recovered.

*Case 14.* (157/1947.) Woman, aged 56. Ill for four months. X-ray treatment on account of a diagnosis of inoperable cancer. Bronchoscopy: Stenosis of second dorsal bronchial branch in right inferior lobe. Microscopy: Carcinoma (admixture?). Sputum maximally 290 c.cm., pre-operatively 20 c.cm. Indication for operation: Mediastinal site of chronic abscess with severe pneumonitis, perhaps bronchial carcinoma. *Right pneumonectomy and oesophageal resection* (JENS L. HANSEN). Considerable infiltration along the oesophagus, which was resected, because ingrowth of carcinoma was suspected. Free pleural space dorsal to the abscess. Size of abscess 3 plus 4 cm. Histological examination: stenosing unspecific bronchitis. No malignancy. Course uneventful. Recovered.

### Pre-operative Treatment, Technique and Operative Tactics.

The patients were treated pre-operatively by postural drainage, with penicillin and sulpha-preparations, and bronchoscopies were undertaken. In one case (6) the abscess cavity was treated directly through bronchoscope with penicillin and alphasol (a neutral sulpha-solution). The principle of procedure is described in a paper by HANSEN & SMIDT (b). In the cases where the time of existence and site of the abscess indicated radical operation the conservative treatment was carried through for some length of time, most often one month. By so doing we succeeded, as stated above, in reducing the amount of sputum rather considerably, and generally also in removing the putridity of the sputum. Simultaneously the patients were given blood transfusions and a diet rich in protein and calories. Odontological and otorhinolaryngological examinations were made in all cases and treatment given if necessary.

The operations were performed in general anaesthesia with tracheal intubation and controlled respiration. The intubation was carried out in local anaesthesia while the patients were awake to prevent the spastic coughing which intubation at the first

stage of general anaesthesia may cause from pressing pus from the abscess into the bronchi. The general anaesthesia was commenced by intravenous injection of evipan, citodan, or narcodorm. ANDERSON, CRAFOORD & FRENCKNER's anaesthesia apparatus was applied. Nitrous oxide, oxygen, and ether were used in the closed system. Curare was used only once in the present series (8). Bronchial tamponade was not applied. Secretion was instead sucked up continually during the operations. In addition pre- and postoperative bronchoscopy was carried out to a great extent.

The thorax was opened by a large dorsolateral incision and excision of a rib from neck to cartilage. The most difficult part of the operation is generally that of detaching the abscess area from the inside of the thoracic wall because of severe synechia in this place. Pulmonary tissue may be completely absent, as is commonly known from pneumotomy. The detaching should in such cases be performed extrapleurally — between the ribs and the parietal pleura — as is done in open intrapleural pneumolysis in cases of tuberculosis. In this layer there is, however, likewise found synechia and often considerable haemorrhage. In case of long-existing processes large anastomoses will sometimes develop between the pulmonary and the intercostal vessels. The abscess cavity was opened during the operation in one or perhaps two cases (6?, 9). In the case where the abscess is known for certain to have been opened (9) there occurred no empyema.

Centrally the dissection is generally rendered difficult by firmly adherent glands and inflammatory infiltration. As a rule, however, the dissection proves easier the further centrally one gets.

Eight of the eleven lobectomies were carried through by dissection, while in three cases a tourniquet was applied to part of the lobe stalk (4, 5, and 12).

In the case operated on within two months of the onset of the disease (6) the dissection was particularly difficult on account of succulent, oedematous tissue right up to the hilus. This case was the only one that was complicated by bronchial fistula.

The bronchial end was in all cases sutured with steel and silk and generally covered by pleura. After dissection and bronchial suturing the remaining pulmonary lobes were detached from the inside of the thoracic wall to allow of as easy and prompt an expansion as possible. This procedure seemed particularly important in cases of upper lobe extirpation.

In one case (11) the abscess was so small that the operation could be limited to resection of the anterior one-third of the right inferior lobe.

Pneumonectomy was done in two cases. In one of these (13) the abscess, proceeding from the superior lobe, had destroyed part of the inferior lobe. In the other case (14) both the course, microscopy of tissue, and findings on palpation revealed features so suspicious of cancer that lobectomy was regarded as too small an operation. The pneumonectomy even had to be supplemented by oesophagus resection. In the other case where a diagnosis of bronchial carcinoma was suggested on the basis of the finding in the sputum (1) palpation during the operation revealed no conditions so suspicious that there was found indication for pneumonectomy.

Sulphathiazole and penicillin were applied in the operation area. In the cases of lobectomy and pulmonary lobe excision drainage from the pleura was undertaken for from two to four days. Thoracentesis was performed after pneumonectomy.

After the operation the patients were given penicillin (since 1945) and sulphathiazole. They were placed in oxygen tent for the first 24 hours, interrupted by carbogen inhalation every hour. They generally stayed in bed about one week after the operation.

## Results.

One patient (8) died postoperatively (cor pulmonale). The two patients with pulmonary tuberculosis (2 and 12) died nine and twelve months respectively after the lobectomy. The direct result of the operation, which had been regarded in advance as a purely palliative, symptomatic operation, was, however, exceedingly satisfactory in both cases. The patients became afebrile and relieved of their profuse, putrid expectorations and haemoptyses. Death occurred probably far later and after a far less harassing illness than if lobectomy had not been done.

Thus, the operation fatality rate was 7.1 %, a figure corresponding exactly to that found by LINDSKOG for primary radical operations.

The eleven patients who are alive and were submitted to follow-up examination from one to three years after the operation were found to be perfectly fit. One of them (6) has a small bronchial fistula excreting 2 to 5 gm. within 24 hours. Her troubles



being inconsiderable she does not at present want to be operated on.

Other postoperative complications were empyema in one case (10) and atelectasis in two cases (3 and 7). The empyema was treated by drainage and complete closure was obtained in the course of three months. The atelectasis was treated by means of bronchoscope on the third or fourth day after the lobectomy and involved no subsequent complications. The duration of the postoperative stay in hospital was under one month for 8 of the 13 patients who survived and up to two months for three patients, while two patients stayed in the Department between two and three months.

Only two patients (with empyema and bronchial fistula) needed out-patient after-treatment, which extended over two to three months. The other patients became able to work after about one month of convalescence after their discharge from hospital.

### Discussion.

Secondary lobectomy after preceding drainage was done in no case in the present series. Other series have been reported in which the operation was extensively performed. Thus, in the series described by VALLE from St. Louis consisting of 244 cases of conservatively and surgically treated pulmonary abscess (208 in adults) there were done 28 secondary lobectomies and 2 pneumonectomies. That secondary lobectomies were not done in the present series is due to the following facts: (1) the primary lobectomies seem to give better results (LINDSKOG). (2) The conservative treatment with chemotherapeutics, antibiotics, autovaccine, postural drainage, and bronchoscopy will most often bring the patients past the acute stage without drainage being necessary for life-saving reasons. This treatment was therefore applied where the result of pneumonotomy was in advance regarded as doubtful. (3) Of secondary operations we have always managed to do with either muscle implantation or the thoracotomy described by HANSEN with radical excision of the walls of fistula and abscess, bronchial suturing, and primary closing, in other words an operation which both involves less risk and leaves behind larger areas of normal pulmonary tissue. It is hardly advisable to do lobectomy immediately after the acute stage of pulmonary abscess, as was done in one case (6). The lymph tracts contain bacteria, and the

tissue is succulent, difficult to dissect, and rather frail for the suturing to hold. Since the uncommonly broad communication with the bronchial tree was thought to contraindicate pneumonotomy the lobectomy ought to have been postponed a few months. The patient's condition at this point of time very well admitted of such a postponement.

### Summary.

Fourteen cases of solitary putrid pulmonary abscess have been submitted to radical operation: pneumonectomy (two), lobectomy (eleven), or partial lobe resection (one) as the primary surgical intervention without preceeding surgical drainage. Two of the patients had cavernous tuberculosis with severe putrid mixed infection dominating the condition. In the remaining cases there were the following indications for radical operation: Duration of the disease, recurrence, severe pneumonitis and haemoptyses, or a site which rendered pneumonotomy risky. One patient died after the operation (cor pulmonale). Operation fatality rate 7.1 %. The two tuberculosis patients improved considerably in the course of the first few months, but died about one year after the operation. The remaining patients recovered and became able to work far earlier than if pneumonotomy had been done.

Radical operation should be the principal treatment where long-existing abscesses are concerned and considered in cases of newly developed abscesses localized high up in the axilla, under the shoulder blade, mediastinally, or in an interlobar fissure. In the latter cases conservative treatment — without pneumonotomy — should, if possible, be extended over several months. Radical operation should be done if the abscess persists or recurs. Radical operation is inadvisable at the acute stage.

### Literature.

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## On Complications in the Treatment of Varices with Etolein. (Etanolamino-oleat.)

By

OLOF OLSSON.

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The ideal remedy in the treatment of varices with injections should have a highly intima destructive and thromboplastic effect, it should not occasion pain at injection and it should not lead to necrosis on happening to be injected paravenously. Etolein possesses all of these desirable properties but there are this notwithstanding observed occasional undesirable secondary effects.

Etolein is an oily fluid consisting of monoetanol-amino-oleinat ( $C_{17}H_{33}COONN_3CH_2CH_2OH$ ) in an aqueous solution and is manufactured by Astra in solutions of 3 per cent and 5 per cent. On mixing with blood this latter is haemolysed and becomes viscid and sluggish. On intravenous injection etolein produces thrombi by injuring the endothelium. In vessels removed 24 hours after the injection of etolein it is in histological sections seen how the endothelium of the thrombosed vessels is frothily swollen, has pyknotic nuclei, and is partially peeled from the internal coat. In vessels removed one to several years after the etolein treatment one can, when the etolein effect has been weak, vaguely distinguish the elastica interna, and the different layers of muscle are easily recognized, while the thrombus is composed of a ridge of connective tissue, but partially fixed to the wall and leaving free a large portion of the lumen. In other cases the musculature is seen to be broken up into smaller or lesser bundles and surrounded by solid connective tissue and the organized thrombus is adherent to the entire or greater portion of the vessel wall. Lumen has an

irregular shape, due to the formation of fresh channels within the thrombus. In other cases in which the etolein effect has been entirely satisfactory the vessels and thrombus consist of a strand of connective tissue in which only a slight trace of the different layers of the vessel wall are suggested. The hereby described changes in the vessel wall are in good agreement with those found at animal experiments on the treatment of rabbit veins with mercuric chloride (9). It is hereby seen that 3 to 4 hours after injection the intima is partly peeled off from the media and is enclosed within the thrombus. Within a day or so the intima is entirely necrosed and inflammatory cellular infiltrations appear in the remaining layers of the wall. On the 9th day the ingrowth of connective tissue is vaguely perceptible in the periphery of the thrombus. Two weeks following the injection the organization of the vessels begins to take place and within one month (small experimental animals) the entire thrombus is invaded by connective tissue, and capillaries.

All media for the treatment of varices have undesirable secondary effects. With reference to the etolein the most important of these are:

1. Periphlebitic reactions.
2. Allergic reactions.
3. Haemolysis of the blood.
4. Coagulation thrombosis and pulmonary emboli.
5. Necrosis at the site of injection.

The *phlebitis* induced varies greatly in degree according to the varying sensitivity in different individuals, but there is also often observed a different reaction at different occasions in one and the same individual. This is evidently due to the fact that the rate of circulation is different in different varices, wherefore the etolein concentration and thus the effect attained vary in degree. The symptoms of phlebitis are, briefly, a more or less pronounced tenderness and swelling, which occasionally reaches such a degree that it prevents the patient from working, and causes a slight elevation of temperature and an accompanying feeling of malaise. There is a considerable difference between the phlebitis induced at percutaneous injection and that following injection of the same amount of etolein through a ureteral catheter introduced into the vessel. Following percutaneous injection the phlebitis never becomes so severe that the patient has

to discontinue his work and it gives rise to actual discomfort only in exceptional cases, in which the injection has been carried out immediately proximate to an ankle joint or a knee joint, where the phlebitis is exposed to a continuous traumatization by the movements of the articulation. Post-operatively, however, one occasionally encounters a periphlebitis so pronounced that it distresses more than the operative wound. The swelling and tenderness reach a maximum on the first and second day after the treatment, then speedily regressing. Those that owing to the phlebitis have had difficulty in walking are already 4 to 5 days after the treatment so much improved that they are able to walk without difficulty and after the lapse of one week they have hardly any discomfort from the varices treated.

The dose of etolein, employed in the treatment of varices, is not toxic in the usual sense of the word. WESTERBORN (4) has on rabbit shown that *dosis lethalis minima* is 100 à 130 mg per kg bodily weight. If these results were applicable to man *dosis lethalis minima* would be about 30 times greater than that used in the treatment of varices. Etolein can, however, in hypersensitive individuals induce *allergic reactions*, with well-nigh every conceivable type of manifestation (5, 7). We have been spared from anaphylactic shock with lethal outcome but one such case has been reported in Sweden:

Male, aged 38, who on several occasions had received varices-treatment by means of injections with various preparations, was operated for his varicose veins at Växiö County Hospital. At a supplementary treatment given by a general practitioner he received an injection of one ampulla of etolein. Immediately after the injection he felt a salty taste in his mouth, coughed up froth, and died in a few minutes. The autopsy (KARLMARK) offered no explanation to the death.

According to our experience of several thousands of cases treated with etolein, allergy reactions occur in about 1 per cent of the cases. The discomfort usually is in the form of malaise and vomitings, appearing one or more hours after the treatment. In the severe cases there are also short fainting spells. In a series (3) of 398 followed-up operated varices-patients three had such discomfort from the injections that etolein had to be discontinued and hypertonic glucose solution used instead. These three cases are of interest in that they represent three distinct types of allergic reaction.

*Case I.* Male, aged 52. Asthma of many years standing. Varices treated with injections 5 years previously, probably with glucose. At the high ligation of the long saphenous vein a high-percentage glucose solution was injected through an ureteral catheter. Only slight malaise at operation. Two days later percutaneous injection of varices with 2 ml etolein. Ten to fifteen minutes after the injection he became nauseated, vomited several times, had cold sweats and prostration, and also slight symptoms of asthma of short duration. He recovered after half an hour and was able to go home. At two subsequent visits at the Clinic the varices were injected with glucose solution without this giving rise to discomfort. At his fourth return, two weeks following the etolein injection he received a percutaneous injection with one half ampulla varicocid. After ten to fifteen minutes he had the same discomfort as following the etolein injection and had in addition a severe asthmatic attack, more violent than he ever previously had had. On the administration of stimulants he soon recovered.

*Case II.* Female, 50 years of age. Absence of allergy in her history. On several occasions treated abroad with injections for varices but does not know what the injections contained. Operation with high ligation of the long saphenous vein combined with etolein injection at operation. Condition good on the day of operation. At discharge the following day she suddenly became nauseated, vomited violently and fainted. The following twenty-four hours she had a very affected circulation. Re-operation one year later with low ligation and etolein injection. The following day she had discomfort similar to that at the previous operation.

*Case III.* Female, aged 37. Absence of allergy in history. At the high ligation of the long saphenous vein 2 ml 5 per cent etolein were injected. On the two days following operation she received a daily injection of etolein. She had no discomfort at or subsequent to the operation until she on the eleventh post-operative day showed an urticaria over the entire body. At intracutaneous testing with 0.1 ml of a 1 per cent solution of etolein the infiltrate in 15 minutes increased to twice its size and three hours later she had an erythema at the site of injection the size of the palm of a hand.

These three cases are of interest not only because the allergic reactions were released in such different organs: Case I the circulatory system + respiratory tract, Case II the circulatory system + the intestinal canal, and Case III the skin, but also in that the reactions appeared at such different intervals after the injection: Case I, ten to fifteen minutes, Case II, twenty-four hours, and Case III, more than a week after the treatment. In Case I one has the impression that there must have been a completed allergy with immediate reaction. This patient was an asthmatic and it could not be entirely excluded that he earlier had received etolein-injections. The form of allergy observed in Case II, with

its appearance twenty-four hours after the treatment, and with identical reactions and intervals on two separate occasions, is reminiscent of the bacterial allergy as in the tuberculin reaction, even though the appearance of the manifestations is different. In Case III there is a picture which in all essentials is in agreement with serum sickness, thus a late reaction of the initial contact with the allergen.

Hypersensitivity to etolein can be tested either percutaneously (patch test) or intracutaneously. The percutaneous test is too time-consuming for use in ambulatory treatment while the intracutaneous test described by WESTERBORN is well suited for this purpose. He injects 0.1 ml 1 per cent etolein intracutaneously and takes the reading after 15 minutes. If during this time the wheal has increased in size or there has appeared an erythema at the site of injection he considers the test as positive. If one by means of the allergy test desires protection against unpleasant surprises it is necessary to make an intracutaneous test in immediate association with each injection, as an allergization may take place at any time during the course of the treatment. WESTERBORN (7) thus mentions two patients with negative intracutaneous test reactions who had shock-like allergic reactions, the one at injection No. 2 three days after the initial treatment, and the other after the 9th injection six months after the initial treatment.

We have for some time used the intracutaneous test but have now discontinued this, as experience has shown that serious allergic reactions are so rare that it can not be considered necessary to subject the patients to this discomfort.

LINSER and VOHWINKEL consider the fatty acid preparations inappropriate for injection because of their *haemolytic effect*. Haemolysis undoubtedly occurs to a certain extent, as is for example seen in varices operation when the etolein is injected retrogradely and the blood leaks out beside the catheter. There has been discussion as to what extent the haemolysis can be made responsible for the discomfort in the form of malaise and vomiting that were mentioned among the allergic reactions.

In order to investigate whether the haemolysis was of such a degree that it should be considered as a disadvantage the author at etolein injections in connection with varices operations took samples of venous blood from the arm five minutes prior to the etolein injection, at this and five minutes and about two hours, respectively, after the injection, and analyzed the plasma for hae-

moglobin. Heparin was used as anti-coagulant. In none of the 11 cases investigated was any haemolysis of the circulating blood observed, although there in all of the cases was haemolysis of the blood taken from saphena magna in connection with the injection. Six of the cases had received 2 ml 5 per cent etolein and 5 of the cases had received 5 ml 3 per cent etolein.

In order to investigate whether conceivably haemolysis might occur if the entire dosage entered directly into the circulating blood, thus not, as in the varices treatment, being deposited in a vascular area more or less suspended from the circulation, some tests in vitro were carried out.

*Test I:* To 1 ml heparinized blood was added 5 per cent solution of etolein in the ratio 1/400 to 1/10.

Heparin blood + etol. in proport.	After 5 minutes.	After 10 minutes.
1/400 .....	0 haemolysis	0 haemolysis
1/200 .....	0    »	0    »
1/100 .....	0    »	Suggested haemolysis
1/40 .....	Suggested hemolysis	Haemol. to 10 %
1/20 .....	Blood viscid, semi-translucent	Blood viscid, semi-translucent.
1/10 .....	Total haemolysis	Total haemolysis

*Test II:* 5 per cent solution of etolein is diluted with saline solution in proportions 1/2 to 1/1024. To 1 ml of these solutions was added 1 drop of heparinized blood.

Etolein sol. + 1 drop of blood.	After 10 minutes.	After 6 hours.
1/2 .....	Marked haemolysis	Marked haemolysis
1/4 .....	»    »	»    »
1/8 .....	»    »	»    »
1/16 .....	»    »	»    »
1/32 .....	»    »	»    »
1/64 .....	»    »	»    »
1/128 .....	0    »	Slight    »
1/256 .....	0    »	Suggested    »
1/512 .....	0    »	0    »
1/1024 .....	0    »	0    »

3 ml 5 per cent, or 5 ml 3 per cent etolein solution distributed in the entire blood volume (6 liter) would correspond to an etolein concentration of 1/2000 of the 5 per cent solution. These trials



show that etolein requires a considerably higher concentration than that reached in the varices treatment before giving rise to a haemolysing effect other than local.

The most dreaded complication in all varices treatment is the *pulmonary embolus*. Earlier when in the operative treatment the patients were permitted bed rest during most of the period of treatment the mortality was not inconsiderable. In larger statistical surveys it varies between 0.25 and 1 per cent. In a statistical survey from Sweden (WESTERBORN, 8) including the years 1928—1934 the embolus mortality following high ligation combined with injection was 0.36 per cent (4 deaths in 1200 cases operated). Today, when the patients are not permitted to remain in bed after the operation the mortality is considerably lower and the incidence of emboli very small. For treatment with injections alone the mortality (8) is about 0.036 per cent (11 deaths out of 30,000 patients treated).

During the 5-years period 1940—1944 there were at our Clinic (both hospitalized and out-patients) operated 1,408 patients, representing 2,132 operated legs (high ligation of the long saphenous vein + etolein injection), and during this same period we used approximately 13,500 etolein ampullae representing virtually the same number of varices injections. In association with these treatments we had no mortalities and observed the following 4 cases of embolus which all recovered.

*Case I:* Male, aged 48. Operation 2. 27, 1940, with high ligation of the long saphenous vein + etolein injection. Discharged two days following the operation. Re-admitted 3. 21 with stitch-like pain in back that persisted about two weeks. Roentgenogram 4. 3 showed absence of parenchymal changes. Was nevertheless interpreted as pulmonary embolus. No signs of thrombosis of the leg. Discharged 4. 11.

*Case II.* Female, aged 46. Had earlier had injections without effect. Was seen 11. 22, 1943 and had at that date had a thrombophlebitis of the right calf for a week. When the phlebitis had regressed high ligation of the right saphenous vein + etolein injection was carried out. During the following week 3 injections were administered, the last on 12. 5. —12. 9 she had a sudden stitch in her back. The patient was seen by a physician in her home 12. 10 and a diagnosis of pulmonary embolus was suggested. She was confined to bed for ten days with fever during the first four days. There was no swelling of the leg.

*Case III:* Female, aged 36. Operation 6. 2, 1944 with bilateral high ligation of the long saphenous vein + etolein injection. Discharged three days after the operation. On 6. 13 a stitch in the right

chest and chills. No coughing. Admitted to the medical service 6. 15. Roentgen showed a small exudate in the right pleura. At puncture 20 ml of clear pale yellow fluid were aspirated. On the night of 6. 23 there arose signs of deep thrombus in the left leg. Received A. P. treatment and was discharged 7. 27 free from symptoms from leg or lungs.

*Case IV:* Male aged 38. In the autumn of 1942 leg ulcer on the left small of the leg. Had 11. 30 1943 an excoriation at the site of the old ulcer. 12. 8 he felt a swelling and tenderness in the left calf. Admission to the surgical service 12. 16. The left calf was then 4 cm greater in circumference than the right. Venography 12. 17 showed a normal filling of both the deep and the superficial veins of the lower leg. The popliteal vein was seen with contrast filling about three fingers breadth proximal to the knee joint. The swelling of the leg soon regressed. The patient received 2 etolein injections in his varices before discharge on 12. 23. 1943. He was free from symptoms from the leg and had only a slight swelling at the site of exposure for the venography. 1. 5 he had a severe stitch in the right chest. Admission to the medical service 1. 7. The left calf was then moderately swollen and he showed signs of a right-sided pulmonary infarction. The swelling of the leg and the pulmonary changes regressed successively but at discharge 2. 8. 1944 the left foot was still rather swollen.

In the first three cases the emboli occurred after high ligation of the long saphenous vein + etolein injection. In none of the cases were there coincident with the embolus signs of a deep thrombosis although this later appeared in Case III. There was probably in all three cases question of a small thrombus at the orifice of the saphenous vein into the femoral vein. In the fourth case the correlatoin between the pulmonary embolus and the varice injection is questionable although it can not be excluded. The negative venography prior to the treatment by no means excludes the presence of a thrombosis in one or more of the small deep veins of the calf. The incidence of emboli in the present series is 0.214 per cent (3 emboli in 1,408 operated patients). If, instead of calculating the incidence of emboli per operated patient, the incidence is calculated per operated leg, it is 0.141 per cent (3 emboli in 2,132 operations). The incidence of embolus after high ligation with injection in the present series, where bed rest after the operation was not permitted, is of the same magnitude as the embolus mortality earlier when the patients were permitted bed rest after the operation.

*Coagulation thrombosis* of the deep veins in connection with varices operation and retrograde injection of sclerosing fluid is an occasional complication. During the years 1940—1947 we have

operated approximately 2,600 patients with ligation and retrograde etolein injection and have seen but two cases of deep thrombosis; one case per annum 1946 and 1947). It is noteworthy that both of these cases were females with disturbances of thyroid function.

*Case I.* Female aged 25. Thyreoid medication for three years for hypothyreosis. Left leg swollen for several years with a circumference 2 cm greater than the right leg, the consistency doughy as in deep varices. Operation 5. 4. 1946 with high ligation of the left long saphenous vein + etolein injection. On the day of operation there was a moderate bleeding from the wound wherefore a pressure bandage was applied. The leg was very tender after the operation but the patient was able to be ambulatory for about 6 hours every day. On 4. 14 the leg was so tender that she was unable to stand on it. 4. 15 she had fever ( $38^{\circ}$ — $39^{\circ}$  C) and on 4. 18 she was admitted to the hospital. She had then, notwithstanding confinement to bed, a considerable swelling of the left lower leg (6 cm wider in circumference than the right leg) and fever ( $38.5^{\circ}$  C). After heparin and A. P. treatment the temperature soon became normal but the swelling was at discharge from the hospital one month later still troublesome. In August 1946 the difference in the circumference of the calf was the same as prior to the operation but she still had pain in the leg. In december 1946 the leg was virtually in the same condition as prior to the operation.

*Case II.* Female aged 46. Operated for exophthalmic goiter in 1931. Varices following parturition 1926. Operation 11. 7. 1947 with high ligation of the right long saphenous vein and low ligation of the left external saphenous vein + retrograde bilateral etolein injection. After the operation she had severe shooting pains in the left popliteal space and 11. 9 the left lower leg began to swell and become indurated. On admission 11. 28 the left calf was  $6\frac{1}{2}$  cm thicker, and the left thigh 3 cm thicker than the right leg at comparable sites. She received heparin and A. P. treatment, the swelling regressed successively and at discharge 12. 15 the thighs were equal in size but the left calf was still 2 cm thicker than the right.

A complication that commonly occurred with the preparations earlier used was *ulceration following paravenous injections*. This is practically never seen when etolein is employed, the only exception being in occasional cases when by accident the injection is made into an indurated pre-ulcerous area of the small of the leg. These lesions are superficial and heal within a couple of weeks. No comparable figures on the incidence of ulceration following treatment with different preparations can be reported if the different preparations have not been used by the same physician. BERTELSEN-DALGAARD (1) presents such a series with the preparations: Na-salicylate 30 per cent, quinine-urethane, and vari-

cocid. With the first two preparations roughly 400 injections had been carried out with 16 and 67 necroses, respectively, and with varicocid 1,200 injections had been carried out with 3 necroses. Etolein is chemically closely related to varicocid. It is our impression that the incidence of necrosis following etolein injections is much lower than that reported for varicocid.

After a marked phlebitis there remains over a couple of months a brownish streak which often distresses the female patients. These streaks, however, always disappear. The dark brown spots, which occasionally appear at the site of injection when the etolein has been injected into a haematoma, or when the etoleinized blood has leaked through the puncture of the vein may, however, persist.

### Summary.

The author discusses the following secondary effects in the treatment of varices with etolein.

1. Periphlebitic reactions.
2. Allergic reactions.
3. Haemolysis of the blood.
4. Coagulation thrombosis and pulmonary embolism.
5. Necrosis at site of injection.

1. The *periphlebitis* are commonly moderate and do generally not keep the patients from working. The degree of this reaction is determined partly by the individual sensitivity and partly by the circulatory conditions of the vessel treated.

2. The etolein may induce *allergic reactions* of widely divergent type but usually they are very mild. The allergy may debut at any point of time during the treatment. Serious allergic reactions are so uncommon that it is not necessary to make any allergy test, if one avoids injections in the case of asthmatics, eczema patients, and other allergic persons.

3. The author shows experimentally that the *haemolysing effect* of the etolein is so small that haemolysis only occurs locally. In order to induce a haemolysis appreciable in the circulation there is required a dosage six to eight times greater than that used at the varices treatment even in the event that the entire etolein dose should immediately mix with the circulating blood.

4. Among 1,408 patients operated during 1940—1944 with high ligation of the long saphenous vein combined with retrograde

injection of etolein there was in 3 cases an occurrence of *pulmonary embolus*, none with a fatal outcome. During the same period of time there were used 13,500 etolein ampullae, correspondent to virtually the same number of varices injections. One case that had received injection treatment without operation had also a small pulmonary embolus. The author establishes that the incidence of embolus in the present series, in which the patients have not been permitted bed rest, is not greater than the incidence of mortality after the same operation, when the patients were permitted bed rest post-operatively. Out of 2,600 patients operated upon for varices there were in 2 cases signs of *deep thrombosis* in association with retrograde etolein injection (none of the 3 embolus cases showed clinical signs of deep thrombosis).

5. There is only a risk of necrosis following paravenous injection when this happens within an indurated pre-ulcerous area of for example, the small of the calf.

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## The Treatment of Congenital Atresia of the Esophagus from a Technical Point of View.

By  
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The outlook for children born with atresia of the esophagus (in nearly 90 per cent combined with a tracheo-esophageal fistula) cf. fig. 1, has entirely changed during the last five years. The mortality has decreased from 100 per cent to 20 per cent (12). This has been achieved partly by advances in the surgical technique, partly by a better understanding of the nutritional problems involved.

In the following some technical points will be discussed in connection with a report of seven cases of our own from the last years, of whom the three last cases had a successful primary anastomosis. For more complete information the reader is referred to articles by HAIGHT (3), HUMPHREYS (4) and by LADD and SWENSON (5); also in the Swedish literature (10). Three successful cases have previously been reported in Europe (1, 5).

Since the report of RICHTER in 1913 (9) the ideal method has been considered to be a one-stage operation with closure of the tracheal fistula and a primary end-to-end anastomosis.

When the distance between the two segments of the esophagus has been too great to allow a direct anastomosis, a multiple stage procedure has been resorted to, including

- 1) Closure of the tracheo-esophageal fistula
- 2) Marsupialization of the upper segment of the esophagus to the side of the neck for drainage of saliva etc.
- 3) Gastrostomy for nutrition, and

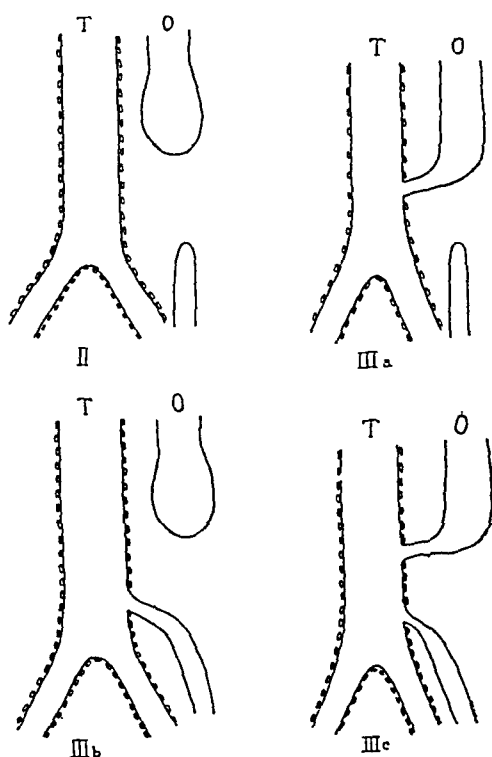


Fig. 1. The different types of esophageal atresia defined according to Vogt. Type I. With absence of esophagus, not depicted. Type II. Two blindly ending segments. Type III. Coexisting fistula to the trachea: a) from the upper segment, b) from the lower segment (the most common type), c) from both segments.

4) Finally, several years later the construction of an artificial esophagus between the two openings.

SWENSON (12) has shown that the direct one-stage procedure can be done in the greater number of cases with a lower mortality than the multiple stage procedure.

### One-stage Procedure With Direct Anastomosis.

The difficulties encountered hereby are:

- 1) the friability of the lower segment with a tendency for the sutures to tear.
- 2) the distance between the segments which puts a constant pull on the suture line.
- 3) the great mobility of the upper segment, which causes an extra strain on the anastomosis every time the child swallows.

Several procedures have been suggested to overcome these difficulties. HAIGHT (2) reinforced the anastomosis by "telescoping" the upper segment around the lower one and obtained good results. SWENSON (12) invented a simple method which seems to be the key to success. With a couple of silk stitches the upper segment is attached to the perivertebral fascia as low down as possible. In this way most of the burden is loaded on the upper segment which is better equipped to carry it, and the extra strain during swallowing is avoided.

The four following cases illustrate the effect of the suggested procedure, the first case being operated before the introduction of the new technique, the others afterwards.

*Case I.* K. L. V. 1318/47. 3-day-old baby boy. Typical story of esophageal atresia since birth. The diagnosis was confirmed by x-ray. Operation 7. 7. 1947 (S—m). Closure of tracheo-esophageal fistula + end-to-end anastomosis of the esophagus. Local anesthesia. The incision was 6 cm, curved between the spine and the right scapula. 2 cm of the third, fourth and fifth ribs were resected. Exposure of the mediastinum. The upper esophageal pouch came down to about 1 cm above the carina. When mobilising the lower segment a small tear occurred in the pleura which could be sutured. The lower segment ended with a fistula to the trachea just above the carina. The fistula was divided and the opening to the trachea was closed with 2 fine sutures. An anastomosis between the two segments was made around a fine rubber catheter with 2 rows, the innermost with fine catgut, the outermost with fine silk. Before closure the cavity was filled with 20 ml saline solution with 30 000 units of penicillin. The child withstood the procedure very well. Milk was given through the catheter. Saliva and mucous could not pass, however, and had to be aspirated frequently. In order to give this secretion a free passage and to avoid damage on the anastomosis from the inlaying catheter this was withdrawn and a gastrostomy was made instead. On the 8th post-operative day there was some secretion from the wound, evidently from an insufficient anastomosis. Two weeks post-operatively the child showed signs of recurrence of the tracheo-esophageal fistula: after the feedings it had spells of coughing and cyanosis. Subsequently there were signs of broncho-pneumonia and the infant expired 3 weeks after the operation.

The autopsy showed that the two segments had separated and that between them an abscess the size of a hazel-nut had formed. From the abscess there was a minute opening to the back of the trachea.

*Case II.* K. L. V. 2275/47. 2-day-old girl. Typical history of esophageal atresia. The diagnosis was confirmed by x-ray, cf. fig. 2. No fever. Hb. 25.6 gm, red blood count 5.82 million, hematocrit 65 %, serum protein 5.6 %. The child was given 150 ml saline solution and 75 ml glucose solution subcutaneously. It was placed in an oxygen tent



and was given penicillin, sulfa and vitamin K. 20 hours later it was operated upon (11. 11. 1947, S—m). Closure of tracheo-esophageal fistula + end-to-end anastomosis of the esophagus. Cyclopropane was given through an intra-tracheal tube without cuff. The incision was 6 cm, curved between the spine and the right scapula. 2 cm each of the third, fourth, fifth and sixth ribs were resected. The pleura was carefully dissected away medially and the azygos vein was divided. Subsequently some air entered the pleura through a minimal lesion which could not be detected. The hypertrophic pouch of the upper esophagus was easily found, big as the tip of a little finger. After some searching the lower segment was found. It was the size of an ordinary lead pencil and opened into the carina. The distance between the two segments was 2 cm. The fistula was divided and the opening of the trachea closed with a running fine silk suture. The upper pouch was mobilized, pulled down and attached to the perivertebral fascia with 2 stitches 000 silk. An incision was made in the lowest portion correspondent to the lumen of the lower segment. An end-to-end anastomosis was made with some difficulty due to the narrow lumen and the tendency of the mucosa to retract. The posterior wall was sewn together with 4 sutures in the muscularis and 2 in the mucosa. The front wall had 3 sutures through all layers and then 2 in the muscularis all 00 000 silk. Now saline solution was injected through the catheter in the upper segment. A small leak could then be observed and was easily repaired with 2 silk sutures. A second injection of saline solution easily passed down into the stomach without any leaking. Then the pleura was punctured and the air withdrawn. The wound was sutured around a small drain. The child's condition following the operation was very good.

On the next day a gastrostomy was performed. 70 ml of serum was given and the following day 20 ml of whole blood (Hb was than 16.6 gm, red blood count 4.62 million, hematocrit 60 % and serum protein 5.9 %). The child had some edema around the eyes and somewhat decreased turgor. The respiration was hoarse and labored. This was improved when steam was introduced into the couveuse.

The following day mother's milk was given in increasing quantities through the gastrostomy. A couple of times the baby belched up a small amount of milk and mucous and one week following the operation it vomited slightly. On the 10th postoperative day the child swallowed a tea-spoonful of water without difficulty and the mother's milk was given orally in increasing amounts. Three weeks postoperatively the gastrostomy was removed and the baby could be put to its mother's breast. On x-ray examination 4 weeks after the operation the passage through the esophagus was entirely satisfactory (fig. 3).

Five months postoperatively the child appears normal in every respect and feeds without difficulty.

*Case III.* K. L. V. 586/48. 1-day-old baby girl was referred from the Maternity Hospital because of cyanosis and respiratory difficulties since birth. The infant's mouth was filled with frothy mucous. The general condition was poor. X-ray revealed an esophageal atresia.



Fig. 2. Case 2 before operation.  
Upper esophageal segment ending at the level of the 2nd thoracic vertebra. Air in the intestine, indicating a tracheo-esophageal fistula.

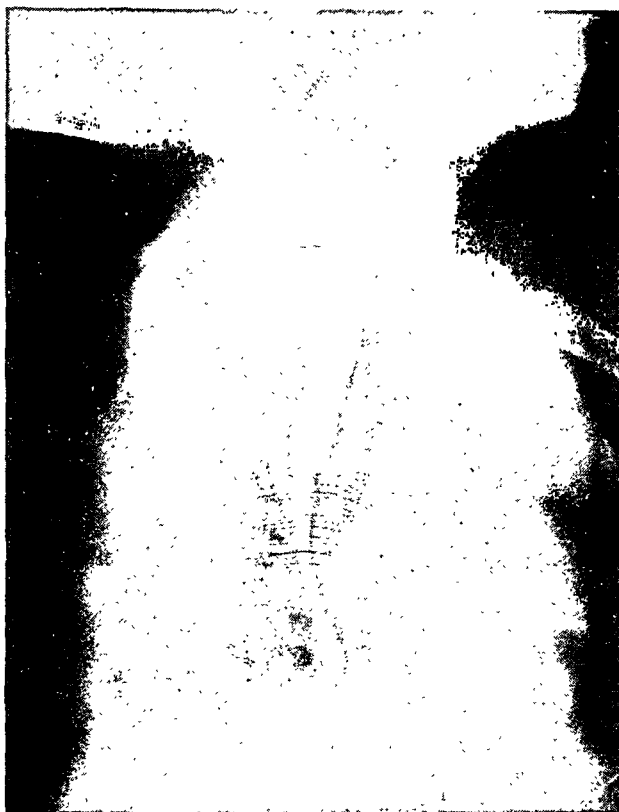


Fig. 3. Case 2 one month after operation.

The upper segment pulled down to level of the 4th thoracic vertebra. Note difference in width between upper and lower segment of esophagus.

After the routine preoperative treatment for a couple of hours the child was operated according to the same procedure as Case II. The upper segment was sited at the level of the third thoracic vertebra. The lower segment was rather wide and well developed up to just behind the carina; from there on it was approximately 5 mm wide and entered the trachea 1 cm above the carina. After the upper segment had been mobilized and attached to the perivertebral fascia it was found that it was possible to anastomose the upper segment to the wide and well developed part of the lower segment with very little tension.  $1\frac{1}{2}$  cm of the lower segment was therefore resected. When the anastomosis was finished fluid was injected into the upper segment under pressure. It passed down easily without leaking. A small drain was left in place. The following day a gastrostomy was done according to Witzel. The stomach was hypoplastic and difficult to get a hold on. During the first two days there was a leak of milk through the wound but the fistula soon closed and on the 12th day the child could swallow without difficulty. An x-ray showed a good passage without any fistula.

*Case IV.* K. L. V. 620/48. 3-day-old baby boy. Typical story of esophageal atresia since birth. The baby was brought to a hospital where an x-ray examination was carried out with a barium meal. He was then referred to us. A nasal catheter was immediately introduced into the esophagus and 5 ml of barium could be aspirated. The esophageal pouch was then carefully irrigated with saline solution. A dangerous aspiration of barium material was thus avoided. After the usual preoperative treatment with fluids, penicillin and vitamin K he was operated upon 20 hours after admission according to the same procedure as Cases II and III. The two esophageal segments ended at the same level, the upper one with a blind pouch, the thin and narrow lower one with the usual tracheal fistula. After the closure of the fistula the upper centimeter of the lower segment was resected because of discoloration suggesting doubtful viability. After the usual fixation of the upper segment an anastomosis was performed without tension. 5 isolated 00000 silk in the posterior muscularis, 6 isolated fine catgut in the posterior mucosa, 3 catgut through both layers anteriorly and finally 2 extra silk sutures in the muscularis. Fluid injected into the upper segment passed down easily without leakage. A tear in the pleura was repaired. Because of this and in consideration of the very satisfactory anastomosis no drain was left. The postoperative course was uneventful. A gastrostomy was done on the 2nd day and on the 10th postoperative day the child was fed orally without difficulty.

X-ray showed a well functioning anastomosis.

### Comment.

These cases illustrate the different outlook for babies with esophageal atresia since the introduction of the new technique. Before being cognizant of this only one case of four was treated

with primary anastomosis and all died, with the new technique three cases have been operated upon consecutively, all with primary anastomoses and all were cured.

In Case I the anastomosis burst and an abscess formed and opened through to the wound. That these events need not prevent an ultimate success is shown by Case III. In fact, in the first successful case in the literature, reported by HAIGHT (2) a complete rupture of the anastomosis occurred. The fistula may heal subsequently; there is said to be a tendency towards the formation of strictures in the future (12). As shown by the present case the greatest risk of a ruptured anastomosis is the re-opening or the fresh formation of a fistula to the trachea. If therefore in the postoperative course an outward fistula develops from the esophagus adequate drainage of the wound is to be ensured. Vomiting should also be avoided. This is best ensured by administering the milk through the ventricular fistula by continuous drip. In a case in which there were signs of recurrence of the tracheo-esophageal fistula LADD (6) re-explored the mediastinum, closed the fistula again and saved the child.

In Case II in which the distance between the two segments was large and the lower segment unusually underdeveloped an uncomplicated healing took place.

The changes in technique that led to success in cases II—IV were

- 1) General anesthesia instead of local anesthesia (which greatly facilitated the operation).
- 2) The avoidance of inlaying catheters through the anastomosis (which endangers the healing by foreign body action and also hinders the swallowing of saliva and mucous) (7).
- 3) The fixation of the upper segment to the perivertebral fascia (most important).

To this the author should like to add as

- 4) A procedure which has been found to be of great value: After the anastomosis is completed fluid is injected with pressure through a catheter into the upper segment. A leak in the anastomosis can then readily be recognized and repaired. Furthermore, the free passage down into the stomach is ascertained.

Cases II, III and IV furnish the answer to another question. It appears from these cases that it is not advisable to resect a

portion of the underdeveloped lower segment in order to be able to place the anastomosis to a wider and stronger lower portion thereof. In Case III in which this was done, giving rise to a slight tension on the anastomosis, this became insufficient and a leakage of some days ensued. In Case II and IV, on the other hand, in which the anastomosis was carried out to very narrow and thin lower segments but, however, with absence of tension, the result has been an excellent anastomosis and a gradual adaptation of the lower segment.

### Multiple Stage Procedure.

Although the first cases of esophageal atresia that were saved (LEVEN, 8), (LADD, 6), had a multiple stage operation as described above, this procedure has turned out to carry a much higher mortality than the direct anastomosis (12). It also means a great deal of trouble and anxiety for the parents of the child, especially during the period of the gastrostomy feeding.

For these reasons we have been seeking some way of establishing a connection between the two segments of the digestive tract in immediate connection with the closure of the tracheal fistula. It seemed closest at hand to transplant a segment of the alimentary canal intrathoracically.

We have had three cases in which the distance between the segments has rendered a direct anastomosis unfeasible or ill-advised.

In the first of these cases a loop of the intestine was used to unite the upper segment of the esophagus with the stomach. The initial intention was to use the jejunum but the mesentery was found to be too short for the purpose wherefore we had to resort to the transverse colon.

*Case V.* K. L. V. 2786/46. Girl, 2 days of age, with typical history of esophageal atresia. After routine preparation the patient was operated upon (1. 1. 1947, S—m). The mediastinum was explored. The distance between the segments was 3 cm and was still greater when the child swallowed. The fistula to the trachea was divided between silk ligatures.

The following day a gastrostomy was done. The next day an anastomosis between the upper segment of the esophagus and a loop of the transverse colon combined with an entero-anastomosis was performed in the following manner: Under local anesthesia the abdominal incision was carried down to the umbilical level. A jejunal loop could not be used due to the shortness of the mesentery. The transverse colon, on

the other hand, was free and of sufficient length. The colon was divided distally to the splenic flexure. There was good nutrition to the transverse colon from the medial colic artery. An end-to-side anastomosis was then performed between the distal loop of the colon and the first segment of the transverse colon. The free loop was brought up behind the stomach to the esophageal hiatus. The operation was then continued through the thoracic incision. The colon was brought up through the esophageal hiatus and anastomosed to the lower portion of the upper esophageal segment without any difficulty. The condition of the patient which had been satisfactory up to this point suddenly became very poor, the heart stopped and could not be made to work again. The intention had been subsequently to perform an anastomosis between the loop of the colon and the stomach and to divide the colon below this point.

In the second case a direct esophago-gastrostomy was tried.

*Case VI.* K. L. V. 219/47. Girl, 6 days of age, with typical history. The infant was extremely dehydrated and had a right-sided pneumonia. After the administration of fluids and penicillin the mediastinum was explored according to the routine procedure. The distance between the segments was 4 cm. The fistula to the lower segment was divided between ligatures.

After deliberation with the parents who doubted being able to co-operate in a treatment with a duration of several years it was decided to perform an esophago-gastrostomy according to SWEET (11), 2 days after the first stage operation.

*Operation:* Left-sided incision at level of the 8th rib curved upwards posteriorly between spine and scapula. Subperiosteal resection of the 8th rib to practically its entire extent. Transection of the 5th, 6th and 7th ribs somewhat posterior to angulus and division of the intercostal muscles. The lower pulmonary ligament was divided. The lower esophagus was exposed and mobilized after division of the covering parietal pleura. The left phrenic nerve was crushed. Incision of the diaphragm from the lateral hiatus to the costal margin. Mobilization of the stomach following removal of the spleen and ligature and division of the short gastric arteries and the left gastric artery close to the cardia. Division of the omental folds. Division of the stomach immediately distal to cardia with double invagination. It is now seen that fundus ventriculi without any tension whatsoever can be approximated to the upper esophageal pouch which is pulled out from behind the left subclavian artery. An anastomosis is performed between the esophagus and the stomach with two rows, silk outermost and catgut innermost. A good and broad anastomosis is obtained. Suture of the diaphragm with fine silk. So far the patient has withstood the procedure well with satisfactory cardiac function, which, however, is deteriorated by the pull on the pulmonary hilus and the pressure on the heart. Adrenalin is injected into the cardiac muscle a couple of times and a favorable effect is obtained by 1 ml glucose intracardially. The action of the heart deteriorates successively, finally ceasing in

spite of intensive cardiac massage and division of the pericardium. It appears, however, that the operation is technically feasible and that in a more favorable case this method may well be used (supplemented with extirpation of the lower esophageal segment).

In Case VII K. L. V. 1430/47 a routine multiple-stage procedure was performed. The patient, however, had a so pronounced hypoplasia of the stomach that a catheter could hardly be sutured into it. After about two weeks the patient showed signs of recurrence of the tracheal fistula and died after two further weeks.

### Comment.

With the favorable results now obtained with direct anastomosis there will probably be less occasion to perform multiple stage operations, especially as SWENSON (12) reports having overbridged distances up to 4 cm with his method of fixation.

In the remainder of the cases, especially where the conditions do not favor a gastrostomy treatment over a period of several years one of the procedures described above may be tried. In my opinion the direct esophago-gastrostomy according to SWEET (11) will have the best prospects of success. A disadvantage of this method is the great hazard still connected with intrapleural procedures in newly born babies.

### Summary.

7 cases of congenital atresia of the esophagus are described.  
4 were treated with direct anastomosis.

The first of them died from insufficiency of the anastomosis, the three others were cured. The advances in the surgical technique in this field are discussed.

3 cases were not fit for direct anastomosis. In order to avoid a multiple stage procedure over a period of years, it was attempted to make an immediate connection between the upper esophageal pouch and the ventricle.

The direct esophago-gastrostomy according to SWEET was tried in one case. Although the child which was in poor condition before operation, died, it seems that this method has the best prospects of success.



The author desires to express his thanks to Dr. Th. Ehrenpreis, associate professor of pediatric surgery, for his valuable collaboration in this work.

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## Plastic Repair of Congenital Esophageal Stenosis.

By

PHILIP SANDBLOM.

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Congenital stenosis of the esophagus seems to be less common than esophageal atresia. In over 13,000 post-mortems BEATTY (2) found only 2 cases. Many stenoses, however, especially of a lesser degree, probably give rise to such slight symptoms that they remain undiagnosed.

While cases of esophageal atresia, usually combined with tracheo-esophageal fistula, are much alike, esophageal stenoses take various forms and may occur at all levels of the gullet. Thus there is reason to assume that the two are caused by different developmental errors. The most plausible explanation has been given by FORSSNER (7), who after extensive investigations came to the following conclusions.

Atresia arises at the early point in development at which the fetal lung buds begin to separate from the fore gut.

Stenoses, on the other hand, arise, like intestinal atresias, at a later point. The digestive canal has then as a result of epithelial proliferation become a solid cord or in any case acquired a very narrow lumen. Subsequently vacuoles appear in the wall, fuse, and thus either form or widen the lumen. It is clear that a disorder in this process may lead to stenoses of the most widely varying types.

British surgeons have shown particular interest in esophageal stenoses. For detailed information see, for example, BEATTY (2). The best systematic classification, by FINDLAY (6), has been based on the nature of the obstruction. Studying his own cases and the

literature, he found among a total of 80 cases 24 in which there was sufficient information given to permit classification. He could then identify the following four types.

1. *Narrowing of the lumen* (9 cases) or smallness of the gullet for a short distance of its length is attributed to a failure of vacuolation of the esophageal wall in the process of development.

2. *A membranous diaphragm* (4 cases) is also assumed to be due to a perversion of vacuolation. A portion of the wall of a vacuole might persist in the form of a diaphragm with a greater or lesser opening either centrally placed or excentric.

3. *Localized fibrous or fibro-muscular thickening of the wall of the gullet* (9 cases), is of unknown etiology.

4. *Spasm* (2 cases) is a disturbance of the coordination in the muscular activity of the esophagus. A cardio-spasm may be regarded as the most common form of this disorder. Although CAMERON (4) found a change in the structure of the *Auerbachs plexus* in such cases, the etiology must on the whole be regarded as unknown.

The portion of the esophagus on the oral side of the stenosis becomes dilated and its wall becomes hypertrophied. It may form a diverticulum as in the cases of JUDD (12), O'BANNON (15), and GROSS (10).

Esophageal stenosis declares itself by difficulty in swallowing and by regurgitation of the food swallowed. This is usually in direct connection with feedings, but food may remain behind, become decomposed, and give rise to inflammatory changes in the wall with resultant increase in symptoms. In addition acute aggravation is often found in catarrhal conditions with swelling of the mucous membranes. Spastic conditions brought on by irritation of the esophagus wall may also cause variations in the course.

In very pronounced stenoses symptoms may appear from birth, but in less severe cases they do not arise until the child begins to take solids. In the cases in which symptoms do not appear until later — possibly not until adulthood — it is probable that a less severe stenosis has been made worse by an inflammatory process. In such cases it would presumably be difficult definitely to establish a congenital origin.

When the clinical picture gives reason to suspect esophageal stenosis, an examination should be made with endoscopy and

x-rays after the administration of a contrast meal. Even with these it may be difficult to distinguish the different forms from one another and sometimes it is impossible to be certain before operation or autopsy.

In differential diagnosis the case history should rule out the possibility of a traumatic or chemical stricture. It may prove more difficult to distinguish a brachy-esophagus with the cardia located in the lower mediastinum. In these cases the x-ray will usually show the characteristic ventricular mucosa below the narrowing. A cardio-spasm with hypertrophy of the musculature in the lowest segment of the esophagus may also give the same picture as a stenosis — 3 cases of STRAUSS's (18) and BEATTY's third case (2) afford examples of the diagnostic difficulties which may be encountered.

A dietary regime with avoidance of solid foods improves the symptoms and may lead to complete freedom from symptoms (SHELDON and OGILVIE, 17). Usually, however, this treatment results in marked undernourishment and under-development. When there has been active treatment it has usually consisted of dilatation with bougies, sometimes complemented by endoscopic division of an obstructing membrane. Lasting freedom from symptoms has been obtained especially in cases with membranous diaphragm (see, for examples, cases in GUISEZ' (9) and VINSON's (20) series and ECKERSTRÖM's case (5).

In other cases this treatment has not led to complete freedom from symptoms. At times it must be continued over a long period or repeated again and again (for examples see SHELDON and OGILVIE, 17). This is particularly true when the obstruction is caused by narrowing of the lumen or a fibro-muscular stricture. Attempts to force dilatation then involve risk of perforation (WHIPHAM and FAGGE, 21).

At times this treatment cannot be carried out at all because of a complicated structure of the narrowing (GROSS, 10) or a firm fibro-muscular thickening. In such cases some form of operation has been resorted to. Surgical intervention is simplest when the stenosis is located very high or very low, making it easier to approach. As early as 1892 BRENNER (3) described a case of high stenosis in which he effected a widening of the stenosis and closure of a tracheoesophageal fistula below it from an esophagotomy on the neck. In 3 cases of stenosis immediately above the cardia, STRAUSS (18), working from the abdomen after drawing the

esophagus down, severed the muscularis down to the mucosa according to HELLER. Two of the cases were restored, while a third died of postoperative complications.

A completely intrathoracic stenosis is more difficult to approach. In 1921 PETERSEN (16) handled a case of pronounced stenosis at the level of bifurcation in which treatment with bougies was unsuccessful. He then constructed an extrathoracic esophagus by pulling a loop of the intestine up under the skin of the chest. Nowadays such a formidable procedure is unnecessary, since excellent results have been obtained by a direct approach with resection and anastomosis as reported by GROSS (10) or with plastic repair as in the following case recently treated at Kronprinsessan Lovisas Barnsjukhus.

(Case no 1936/1947). Girl, 10 months of age. Frequent vomiting since birth. After somewhat more solid food was introduced at c. 4 months of age, she usually did some vomiting at every meal.

On August 8, 1947, when 9 months old, she was admitted to the Children's Department of Akademiska Sjukhuset, Uppsala. She then had acute pharyngitis with a fever of 39° C. In connection herewith her difficulty in swallowing had increased markedly and for some days before admission she had not accepted any food or fluids.

As she recovered from the pharyngitis, her difficulty in swallowing decreased. She could take gruel but regularly regurgitated more solid food. Some improvement was noted after administration of methyloscopolaminii nitras 0.0001 g.  $\times$  4.

The case history revealed no occasion on which the patient had digested caustics.

X-ray examination after an opaque meal (Fig. 1) showed that the contrast passed freely down to the stomach at the beginning of the examination. After larger quantities were given, a stenosis was seen on the border between the middle and lower third of the esophagus. It was only a few millimeters wide and c.  $\frac{1}{2}$  cm long. The esophagus was distended both above and below the stricture. On this filling the contrast did not pass down to the stomach. Above the stenosis some remains of food could be seen.

The child was not in very good condition, with somewhat reduced turgor. She weighed 8 610 gm (weight at birth 4 300 gm).

The patient was transferred to the Surgical Department, Kronprinsessan Lovisas Barnsjukhus for treatment. Because of the firmness and rigidity of the stenosis no attempt was made at dilatation and an operative plastic was decided on.

*Operation, October 2, 1947 (SANDBLOM).*

Intratracheal cyclopropane anesthesia. Right posterior retropleural approach using a vertical incision between the spine and the scapula, bending outwards below the scapula. Subperiosteal resection of about 2.5 cm of the 4th to the 7th rib close to the transverse processes. The

pleura was dissected medially and the azygos vein divided. A branch of the vagus nerve ran around the stenosed esophagus and had to be divided to facilitate approach. On the spot indicated by the x-ray there was a distinct stenosis, a fibrous induration of the muscularis 1.5 cm thick. A simple plastic of the stenosis according to Heineke-Mikulicz was done as follows. A vertical incision about 2 cm long was made through the stenosis into the lumen. This incision was sutured transversely, making a broad passage. 2 rows of sutures, using 5—0 silk, were placed, the knots in the innermost row on the inside, while the outer row was stitched in such a way that the muscularis was adapted without inversion. Before the incision was closed a sound was passed down to the stomach to make certain that there was no essential obstruction in the lower esophagus. After completion of the suturing, a catheter was introduced into the upper part of the esophagus and saline solution injected under pressure. The fluid went down easily, without leakage. The operative field was drained with a small tube. The rest of the wound was closed after the cavity had been filled with penicillin solution. The patient showed no ill effects after the operation, in the course of which she had received 100 ml of blood intravenously.

The next day a gastrostomy according to Witzel was performed under ether. The patient was immediately given nourishment via the gastrostomy.

The postoperative course was without complications. After three days the patient had no fever. The wound healed rapidly. After 2 weeks, nourishment by mouth was begun and as the patient swallowed without difficulty, the gastrostomy could be closed 10 days later. 1 month after operation she could swallow semi-liquid food without difficulty. X-ray examination (see Fig. 2) showed that the stenosis was widened. About half a year after the operation the patient again began to have difficulty in swallowing and was re-admitted to the Children's Clinic in Uppsala. X-ray examination (see Fig. 3) showed a very wide passage at the site of the old stenosis, but a very narrow passage just above the cardia. Endoscopic examination revealed a fold on the left side, about 17 cm below the teeth. This fold offered no noticeable resistance when a no. 18 bougie was passed. It was considered that the difficulty in swallowing was due to faulty coordination within the musculature of the esophagus — i. e. a spasm. After this examination the patient was completely free of symptoms. She has taken semi-solid food without difficulty and showed a normal increase in weight. At X-ray examination 10 months after operation (see Fig. 4) the dilatation of the esophagus has decreased and the spastic stenosis is less marked.

### Comment.

The history of this case is typical of an esophageal stenosis and illustrates the increased difficulty in swallowing experienced when solid food is introduced. It also shows how the symptoms become worse when there is an upper respiratory infection.

The nature of the stenosis was a localized fibrous thickening of the wall of the gullet, FINDLAYS's Type 3. Similar cases have been described by WHIPHAM and FAGGE (21), HUTCHISON (11), SHELDON and OGILVIE (17) and FINDLAY (6).

In these latter cases the nature of the stenosis was studied in post portems, all the children having died before the age of 6 following wasting or attempts to dilate the stenosis.

No doubt other cases of the same kind have been treated with more success, but it seems natural that cases with hard fibrous rings should offer more resistance to dilatation therapy than cases with a membranous diaphragm or a spasm. ASHBY (1) says: "The stricture should be dilated up carefully at regular intervals. With this the children generally and anyhow for a time keep fairly well. Directly the dilatation is left for more than 2—3 weeks the vomiting starts again."

Such cases are probably better helped by an operation of the kind described. The quick and permanent relief offered by this method is in contrast to the long and tedious treatment with bougies. KAY (13) has come to the same conclusion as regards the treatment of cardiospasm in adults. In a series of 17 patients whose condition was not significantly improved by dilatations, complete and permanent benefit was obtained with a transpleural cardioplasty performed in a manner very similar to the operation in the case described above.

*Operative Procedure.* The retropleural posterior approach used in this case was originally described by MIXTER (14) and nowadays is generally adopted in esophageal atresia operations. It provided excellent exposure and there was very little post-operative trouble.

The writer questions whether the transpleural approach recommended by GROSS (10) has sufficient advantages to outweigh the risk of opening the pleural cavity.

The stenosis itself may be treated either by resection and end-to-end anastomosis as recommended by GROSS (10) or by the simple type of plastic repair used in the case reported here. When the latter procedure is feasible it probably involves less risk of sutural insufficiency.

A stenosis of greater length would probably have to be resected and repaired either by an end-to-end anastomosis or, if the distance were too large, an esophago-gastrostomy as employed by SWEET (19) in the treatment of extensive cicatricial obliteration.



Fig. 1. Stenosis with dilatation above and below operation.



Fig. 2. Stenosis widened and dilatation less pronounced one month after operation. Tendency to stenosis at level of hiatus.



Fig. 3. 6 months after operation the operated stenosis is very wide but that at the level of the hiatus is marked and there is increased dilatation above it.

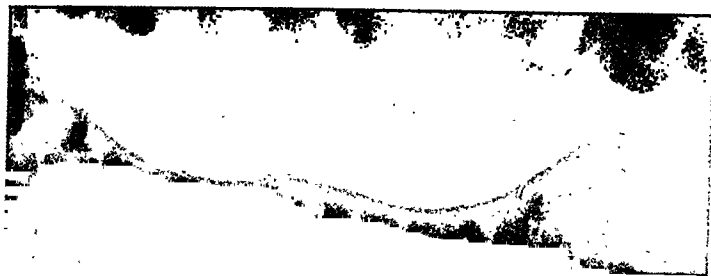


Fig. 4. 10 months after operation the dilatation has decreased.





The writer recommends the method described here of testing the security of the anastomosis by injecting saline into the esophagus under pressure.

It should be pointed out that in some cases a simple incision of the stenosis down to the mucosa might be sufficient and would be extremely safe.

In the case described there was still another stenosis farther down, on the level of the hiatus. Its changing appearance on different occasions and the ease with which sounds were passed through it indicate that it was spastic in type. The site of this stenosis (on the level of the hiatus, just above the cardia) seems to be common in spastic conditions; see the 3 STRAUSS cases (18), SHELDON and OGILVIE, case 8 (17), BEATTY, case 3 (2). It is possible that this lower stenosis is secondary to the upper one.

### Summary.

In cases of esophageal stenosis not suited to simple dilatation with bougies or in which such treatment does not give satisfactory relief, the method of choice seems to be an operation with partial resection and end-to-end anastomosis as described by GROSS or plastic repair as described in this article.

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## On the Surgical Treatment of Hyperparathyroidism.

By

KAARE LIAVAAG.

The first description of a parathyroid adenoma that can be accepted today was probably that presented by ERDHEIM in 1903. In 1904 ASKANAZY associated parathyroid tumors with skeletal lesions. However, it was not until 1926, when the first surgical removal of a parathyroid adenoma was made by MANDL, in a patient suffering from osteitis fibrosa generalisata, and clinical improvement was seen, that practical interest in these related maladies was stimulated.

According to COLLIP, the action of the parathyroid hormone is on the solution of the calcium salts from the bone. According to AUB it is the phosphorous metabolism that is involved, the hormone promoting an increased output of phosphates in the urine. This will result in a hypercalcemia. Anyway, whatever the mechanism may be, the result of a hyperfunction of the parathyroids is the same: hypercalcemia, hypophosphatemia, hypercalciuria, hyperphosphaturia. When this condition has lasted for a while, skeletal symptoms develop, osteitis fibrosa generalisata or general osteoporosis, associated with symptoms from the urinary tract. The latter are due to a hypersaturation of the urine with calcium salts, resulting in calcareous deposits in the renal parenchyma — *i. e.*, a nephrocalcinosis — or concrements in the urinary passages. The clinical picture of this condition which is the result of an overproduction of parathyroid hormone, and which is called primary hyperparathyroidism, must be considered as familiar, and

will not be discussed in this paper. However, there are several features as to this condition that still are obscure. Hence as many cases as possible should be reported in order to throw some light upon the problem, in particular in view to the pathologico-anatomical picture. According to American investigators (ALBRIGHT, COPE, CASTLEMAN, MALLORY, CHURCHILL, BLOOMBERG, BLACK, RANDALL, NORRIS) the following types of hyperparathyroidism may be differentiated:

- 1) Primary hyperparathyroidism due to a focal hyperplasia, seldom in more than one of the glands (adenoma).
- 2) Primary hyperparathyroidism due to a diffuse hyperplasia of all the parathyroids.
- 3) Carcinoma with associated hyperparathyroidism.

As a special group there is the secondary hyperplasia which may affect all the parathyroids in the case of osteomalacia, renal rachitis, and protracted chronic nephritis. However, this hyperplasia is the result of a compensatory mechanism which probably sets in in order to increase the output of phosphate in the urine. However, a clinical hyperparathyroidism in the true meaning of the word is not present in this condition.

Malignant tumors of the parathyroids may be seen, but this is a rare occurrence. NORRIS, in 1948, collected 41 cases from the literature. However, he accepts only 15 of these as carcinomas. Seven of these cases showed clinical evidence of hyperparathyroidism. In Norway the first case of carcinoma of the parathyroid with associated hyperparathyroidism has recently been published by FRETHEIM and LANGE. The usual adenomas show a considerable degree of pleomorphism, sometimes growth with tendency to invade the capsule. This has led to some investigators classifying this condition as a first grade carcinoma (ALEXANDER et al.). According to NORRIS, this serves no purpose because clinically the adenomas must be considered as benign tumors.

With regard to the first group the above mentioned American investigators state that the adenomas, or the focal hyperplasia as they also are called, exhibit a great variety of cells, although the "chief cell" and its varieties constitute the vast majority of the cells. CASTLEMAN and MALLORY found no adenomas entirely composed of the "water-clear cells", or oxyphil cells. The chief cells were the only cells constantly found in the adenomas. NORRIS has examined 1,665 normal parathyroids. He describes six different types of cells (primordial cells, vesicular cells, clear cells, dense

cells, dark cells, oxyphil cells). NORRIS points out that all these cells may be found in the adenomas. However, in some adenomas one type of cells may predominate almost to the exclusion of others, while in other tumors the cells have been mixed in varying proportions and include all manner of transitional forms. An adenoma made up of entirely oxyphil cells is exceedingly rare. The adenomas are usually solitary. In a survey of 322 cases NORRIS found multiple adenomas in 6.2 per cent of the cases.

In the case of diffuse hyperplasia, where all the parathyroids are involved, the anatomic picture is constant: large clear cells, dominating the microscopic picture. In some areas acinar grouping may be seen. The cells are much larger than the other cells of the parathyroid, their diameter varying from 10 to 40 microns. ALBRIGHT et al. do not consider this so much as a hyperplasia but think that it is a hypertrophy of each individual cell. The reason for the appearance of the large cells should be an increased hormone production. The gland tries to hold back the hormone, hence the swelling of the cells.

In the case of secondary hyperplasia the essential feature is the hyperplasia of the chief cells.

According to American authors, about 10 per cent of the cases of clinically demonstrable hyperparathyroidism can be traced back to a diffuse hyperplasia of the water-clear cell type, while 90 per cent of the cases are said to be due to adenomas. According to NORRIS 322 cases of adenoma had been published up to 1946, and according to BLACK and RANDALL 26 cases of hyperplasia up to 1947. This American concept, however, is not held by other investigators. BERGSTRAND has emphasized that there is no essential difference between hyperplasia and adenoma. He points out that all cases are adenomatous hyperplasias, as well where primary as *secondary* hyperplasia are concerned. This question being of considerable interest as to the surgical management, particularly in view of the surgical approach, it is of importance that all cases that might throw some light upon the problem are reported. This is the reason for publishing our material. Should the concept held by American investigators be right, the following procedure should be adopted: If at the operation a frozen section shows adenoma, this should be removed. Multiple adenomas being exceedingly rare, no further search is necessary. One just has to watch the postoperative course and wait and see if not the Ca and P values return to normal. If not, as very seldom, the patient

must be re-operated. A careful exploration for an eventual adenoma is no small operation indeed, as every place where an adenoma may be located must be explored. A half-made exploration is worse than no exploration because it leaves scar tissue without the presence of other tumors being excluded, and may only serve to complicate a re-operation. If the frozen section shows a hyperplasia of the water-clear cell type, a diffuse hyperplasia of all the parathyroids is most likely the case (adenoma with a preponderance of water-clear cells cannot definitely be excluded in the frozen section). In such cases a sub-total resection of the parathyroids must be performed. Three of the glands should be removed, and the fourth, if not much enlarged, should be left. Should also the fourth gland be enlarged, parts of it must be excised. According to BLACK and RANDALL 30 to 200 mg should be left. If more is removed, permanent tetany may result, and if too much is left, the symptoms will usually persist.

The cause of the primary hyperparathyroidism is unknown. An overproduction of a parathyroprival hormone by the pituitary gland has been considered, but has never been proved. If the American dualistic concept is right, the cause is probably not the same in both instances. The term primary hyperparathyroidism is not correct in the case of diffuse hyperplasia, because this condition is interpreted as secondary to a hormonal dysregulation of other endocrine glands. If the so-called adenomas really are neoplasms, this condition might very well be called primary hyperparathyroidism.

### The Material.

During the period 1938—1947 seven cases of hyperparathyroidism have been treated in our department. The age of the patient, sex, number of tumors, location, skeletal changes, renal involvement etc., are shown in the table. (Table I.)

*Sex.* There are 5 females and 2 males. As in other materials, the sex incidence shows a preponderance in females over males. The ratio is stated to be 3 to 1.

*Age.* The age of the patients has varied from 22 to 57 years. In NORRIS's material the age varied from 14 to 57 years, but 70 per cent of the cases were found in the age group 30 to 60 years. During the last years the incidence has accumulated in the younger

Table I.

Case nr.	Sex	Age	Duration	Number of tumors	Localisation	Measurement of tumor	Skeletal changes	Renal stones or calcification	Pathologic-anatomic finding.
1. 1246/41	F	56	15 y	Three enlarged glands			+	+	"Water-clear" cell hyperplasia
2. 5089/41	F	41	1 y	1.	L. L.	Hazelnut	+	+	Adenoma
3. 2001/46	F	35	6 y	1.	L. L.		÷	+	Adenoma
4. 12872/46	M.	22	9 m	1.	L. L.	Hazelnut	÷	+	Adenoma
5. 5557/47	M	52	8 y	Three enlarged glands			+	+	"Water-clear" cell hyperplasia
6. 66855/47	F	51	16 y	1.	L. L.	Hazelnut	+	+	Adenoma
7. 11443/38	F	44	3 y	1.	Ant. mediast.		+	÷	Adenoma

age groups, probably owing to the condition being diagnosed at an earlier stage.

*Single and multiple adenomas.* There were 5 cases of adenoma. In the four cases where the adenoma was found, the Ca and P values returned to normal after the operation, so it should be justified to believe that one adenoma only has been present in these patients. In one patient the adenoma was not found at the first operation. This patient was re-operated by Dr. Nicolaysen at Drammen Hospital, and the adenoma was found in the anterior mediastinum. Also in this case the adenoma was a solitary one. Four of the adenomas we found were located in the region of the left inferior glandule. According to NORRIS (322 cases) adenomas are about equally frequent on the right and on the left side of the neck, although a remarkable difference becomes apparent as to involvement of the superior and inferior glandules, 80 per cent being situated in the region of the inferior, 20 per cent in the region of the superior glandule. An aberrant localisation of the adenoma is found in 10 per cent of the cases. In our material this was only seen in one of five cases. As to the aberrant position 60 per cent of these tumors are situated in the anterior mediastinum, 30 per cent are embedded in the thyroid, the rest being found in the posterior mediastinum, usually retro-

esophageally. This may be a lead as to the succession in which to search for the tumor at the operation.

Two of the cases presented diffuse enlargement of three of the parathyroids. One of these cases was operated on two times. At the first operation two enlarged glands were removed. No clinical improvement followed. The patient was then re-operated, and this time a large gland was removed on the other side. Following this operation the Ca and P values returned to normal. The case has been reported at a staff meeting in Oslo as a case of multiple adenomas. A re-study of the sections shows that there is a diffuse hyperplasia of the water-clear cell type in all the glands. In the fifth case three enlarged glands were removed at the primary operation, all presenting the picture of the water-clear cell type hyperplasia. The four cases of adenoma were all hyperplasias with preponderance of the chief cells as shown in fig. 3.

Our cases thus correspond to the American concept and classification as to the pathologico-anatomical picture. As mentioned, objections have been made as to this classification (BERGSTRAND). In *Acta med. Scand.* Vol. 128, p. 103 HAGTVEDT and MATHIESEN report an interesting case that they think contradicts the American concept. The patient was operated for hyperparathyroidism in 1936, and two adenomas of the chief cell type were removed. The blood calcium value which prior to the operation was 20 mg per cent, returned to normal after the operation, and remained normal except on a single examination in 1943, when it was 12.2 mg per cent. Prior to the operation the patient suffered from renal insufficiency associated with chronic uremia with urea contents varying from 77 to 100 mg per cent. No change was seen as to this, and the chronic uremia persisted. The patient died from an accident on the New Year's Eve 1944. At autopsy 3 enlarged parathyroids were found in the neck. Microscopy showed hyperplasia of the chief cells in two of the glands. In the third there were some areas where also the water-clear cells were seen to be hypertrophied. HAGTVEDT and MATHIESEN think that the hyperparathyroidism in this case has relapsed, all the glands being hyperplastic. Furthermore, based upon the microscopical picture, they think that the case contradicts the American concept. However, this case is obscure. The Ca and P values, four months prior to death, were 8.7 and 2.3 mg per cent, respectively. These figures taken into consideration the diagnosis hyperparathyroidism



is not justifiable. The only ample proof we so far have as to the presence of hyperparathyroidism is the Ca and P values in the blood, and the figures recorded do not permit the diagnosis hyperparathyroidism. The hyperplasia in the case of this patient has probably been related to his renal disease. Secondary hyperplasia of the parathyroids may occur in chronic renal disease. However, it may be objected that the renal insufficiency in this case was not so marked that it would cause such a retention of phosphorous that the Ca values would be affected, resulting in an increased activity of the parathyroids. The clearance was 37 per cent of the normal. However, this was on April 4th, 1943, *i. e.* 20 months before the patient died. There are thus no figures indicating the renal function at the time when death occurred. The mechanism of the secondary hyperplasia in renal insufficiency is still obscure. If AUB's theory as to the effect of the parathyroid upon the output of phosphate in the urine is right, it should be justified to assume that even a moderate retention of phosphate would irritate the parathyroids to an increased activity resulting in hyperplasia. In the case of mild forms of renal insufficiency it might be assumed that the hyperplasia would compensate the tendency to phosphate retention so that the P values would be normal. If the above mentioned patient had lived until he had died from his chronic renal disease, the serum P values would most likely have been increased before death, and the three glands would then probably be taken for a secondary hyperplasia. The microscopic picture, too, would be in favour of this. The case is a very interesting one and gives rise to a series of theoretical considerations, although it cannot be said to be quite clear. In my opinion HAGTVEDT and MATHIESEN have drawn too wide conclusions when they state that the case contradicts the American concept and classification. In the discussion of multiple solitary adenoma NORRIS also states that adenomas and secondary hyperplasia are often mistaken for each other, and CHURCHILL warns against a too radical operation in cases with renal insufficiency. (Fig. 1, 2, 3.)

*Symptoms from the urinary tract.* Six patients had symptoms from the urinary tract. Three patients (no. 3, 4, and 5) had suffered relapses of renal calculi for months and years. In one patient (no. 1) a large stone was found in the renal pelvis. One patient (no. 6) had suffered attacks of renal calculi 15 years previously. Examination now revealed a diffuse nephrocalcinosis with

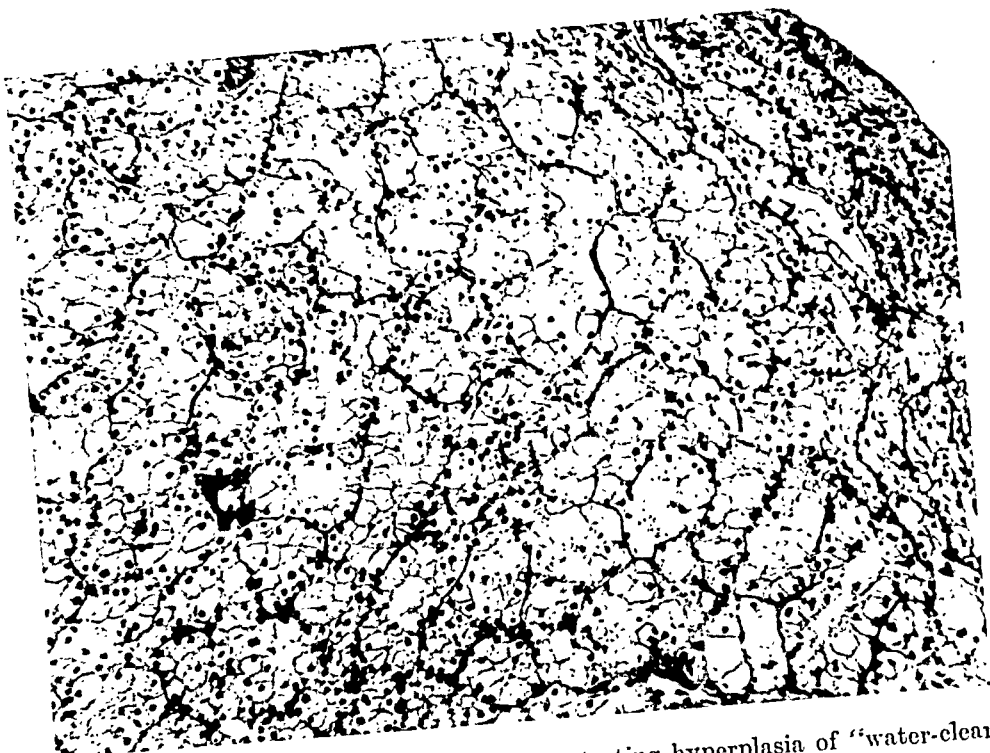


Fig. 1. Photomicrogram from case 1. demonstrating hyperplasia of "water-clear cells" in acinar arrangement.

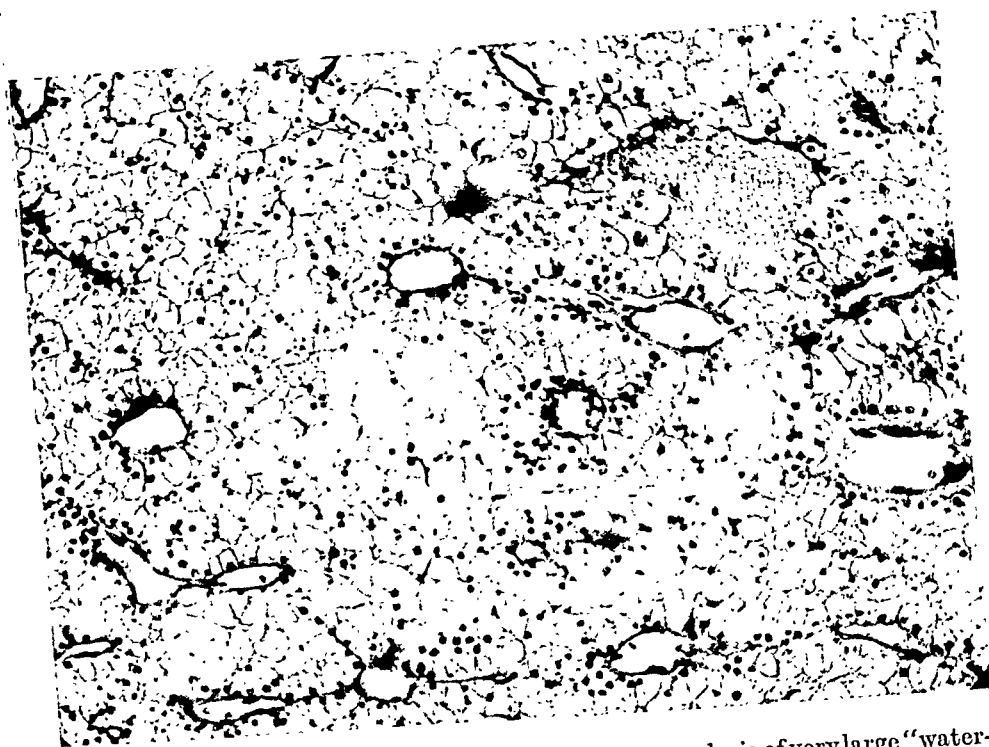


Fig. 2. Photomicrogram from case 5 demonstrating hyperplasia of very large "water-clear cells".

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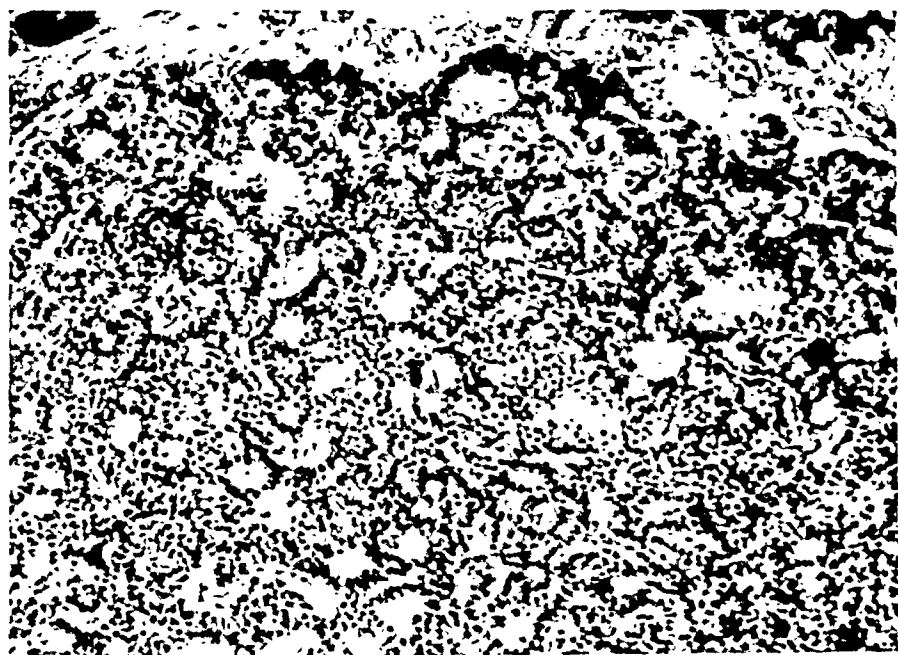


Fig. 3. Photomicrogram from case 2 demonstrating an adenoma of chief cell type.

calcification of the renal parenchyma. One patient (no. 2) had a chronic uremia with a considerable impairment of the renal function, but no concrements were seen on the roentgenogram.

*Symptoms from the osseous system.* Five patients presented symptoms from the osseous system. One of them (no. 1) had a general osteoporosis, and three (no. 1, 6, and 7) had osteitis fibrosa generalisata with multiple cysts and areas of rarefaction in the bones. One patient (no. 5) had a maxillary tumor of the giant-cell type.

One patient (no. 2) developed symptoms of an acute psychosis which was what led to the diagnosis being made when the patient was admitted to an asylum. Dr. EITINGER has given an account of the psychiatric aspect of this case.

From a clinical point of view different forms of hyperparathyroidism have been differentiated, viz., the osseous, the renal, and the gastrointestinal form. Both the skeletal changes and the symptoms from the urinary tract may be regarded as complications to the hyperparathyroidism. The incidence of these complications vary in different materials. In the material collected by NORRIS skeletal involvement was seen in 90 per cent of the cases, and symptoms from the urinary tract in 36 per cent. The incidence of skeletal symptoms being so high in this material may be due to the fact that a large part of the material lies far back when advanced cases only were diagnosed. COPE states that complications from the urinary tract are more frequently found than skeletal changes. Furthermore he holds that the purely renal forms most often are found in mild cases of hyperparathyroidism while skeletal changes are preferably seen in the more severe cases. ALBRIGHT, BAIRD and BLOOMBERG hold that the degree of skeletal involvement is an expression for the duration of the disease rather than for its intensity.

In our material, as it will be seen, involvement of the urinary tract is as frequent as skeletal involvement, and two patients presented renal symptoms only. Preoperatively they had Ca values of 12.2 and 13.3 mg per cent, respectively, *i. e.* considerably lower values than in the case of the other patients, so that one must consider that these cases have been milder forms according to COPE's concept. The most marked skeletal changes in our material were seen in a patient where the condition had lasted for 16 years. With regard to the duration of the disease it may be

Table II.

Case	Ca	P	Phosphatase	Ca output in urine
1	15.0—14.5 mg %	2.05—2.5 mg %	10—20 B. E.	450 mgr.
2	15.4—14.7 "	6.55—5.05 "	5.35 "	50—75 mgr.
3	12.2—11.8 "	2.2—2.3 "	4.1—2.8	420 mgr.
4	13.3—12.8 "	2.4—2.2 "	3.4	
5	14.2 "	2.2 "	3.0	650 "
6	15.6—14 "	1.9—2.5 "	7.7—7.5	230 "
7	15.2—13.5 "	3.0—2.2 "	25	

added that in NORRIS's material it is stated to be from 5 to 7 years. However, ALBRIGHT, AUB and BAUER, in 1934, reported a case where the condition had probably lasted for 39 years. One of our patients had nephrolithiasis 16 years previously, and one giant-cell tumor 15 years previously. In the remaining group the symptoms have lasted from 9 months to 8 years. The patient who had had symptoms for 9 months only, these were only from the urinary tract.

Another problem is that as to the incidence of hyperparathyroidism among patients with renal calculi. Our material is not suited for such an investigation because it consists of selected cases. COPE et al. report an incidence of 10 to 15 per cent. However, this has been corrected to 3 per cent in a later publication. But other investigators find considerably lower figures.

The combination hyperparathyroidism and renal calculi is a so frequent occurrence that in all cases of relapsing calculi it is indicated to determine the Ca and P values in the blood, especially if analysis of the stone shows that this consists of calcium phosphate. (Table II.)

*Preoperative Ca and P values.* These are shown in table II. It is seen that the Ca values have varied from 12 to 15.6 mg per cent. The P values have been low in all cases except case 2 where it was 6.5 mg per cent. This patient had a considerable renal insufficiency, which well may have been responsible for the P value being increased above normal. Two cases (no. 1 and 7) showed considerably increased and one case (no. 6) moderately increased phosphatase values. All these patients presented marked skeletal changes. The phosphatase value is an expression for the activity of the osteoblasts, and it is raised in cases where there is an increased formation of new bone besides the bone destruction.

The excretion of Ca in the urine is also shown in table 2. As it appears, considerable amounts were excreted in the case of patient no. 1 and 3, and 5, while the excretion was more moderate in the case of patient no. 6. The largest excretion, 550 and 650 mg, respectively, was seen in the case of the two patients with hyperplasia. Patient no. 2 had a very low excretion varying from 50 to 80 mg, in spite of the fact that there was a considerable hyperparathyroidism with blood Ca values of 15.4 mg per cent. This patient had a considerable renal insufficiency, and the findings correspond to the experience of other investigators, that when renal insufficiency occurs, the renal excretion of Ca decreases to normal or even subnormal values, while the Ca excretion in the feces increases so that the patient remains in the same state of negative Ca balance.

In case 1 and 3 some tests were carried out as to the Ca balance. In both cases a negative balance was found.

*Postoperative course.* The mortality following operative treatment of hyperparathyroidism is stated to be about 5 per cent (NORRIS). None of our patients died as a result of the operation. In all cases except case 2 there was only slight postoperative reaction. In this case there was a considerable impairment of the already marked renal insufficiency, and the urea content rose to 350 mg per cent and a marked acidosis developed (cf. CHURCHILL's warning of not to be too radical in cases with renal insufficiency).

Otherwise it is the postoperative tetany which is a threat to these patients. A rapid fall of the Ca content to normal or subnormal values are often seen. Whether the patient will show symptoms of tetany does not entirely depend on the absolute Ca values, but also on how rapidly the fall takes place. If the fall takes place rapidly from highly increased values, the patient may develop clinical symptoms of tetany even if the Ca values are normal. It is recommended, therefore, always to give Ca the first postoperative days. In some cases, however, there is a fall to subnormal values with tetany. There are two forms of this tetany. One is the form that appears when too much parathyroid tissue is removed at the operation, and this tetany often becomes permanent.

The other form is characterized by transient low Ca values following the removal of an adenoma. There are two theoretical explanations as to this entity. One is that the other parathyroids on account of the adenoma are depressed in their function, and

a certain time is taken to restore the function. The other theory is that during the first postoperative days there is a back-flow of Ca from the blood to the osseous system, this back-flow being responsible for the fall in the Ca values in the blood. This re-calcination should especially be seen in cases where the phosphatase values are raised. Some authors (CHURCHILL, HELLSTRÖM) recommend to operate in several stages in these cases, therefore. Case 1, where the phosphatase values were markedly raised was operated in two stages because the condition at the first operation was interpreted as an adenoma. The patient showed no symptoms of tetany. Case 6, who had moderately rised phosphatase values showed slight symptoms of tetany, and so did also case 3 where the phosphatase values before the operation were normal. None of these patients had Ca values under 8 mg per cent. Patient no. 5 developed a manifest tetany with Ca values as low as 4.2 mg per cent. In this patient all parathyroid tissue in the neck was removed because of the report on the frozen section which for two glandules read: "not parathyroid tissue". The last enlarged gland which was found, was thus thought to be an adenoma and was entirely removed. When discharged, the patient still had sub-normal Ca values and Ca and D<sub>2</sub> medication had to be continued.

*Late results.* The further fate of the patient depends to a certain degree on how early the diagnosis is made. If irreparable changes have developed in the kidney regression will not occur, and the patient will sooner or later die of his renal disease. However, cured for his parathyroidism, the patient may live for years without any progression being seen. In the case of adenoma, surgical removal of the adenoma will usually give permanent cure. In all our cases the Ca values returned to normal following the removal of the adenoma. Also the P values rose to normal. In patient no. 2 where there were increased P values prior to the operation, an additional increase to 8 mg per cent was seen following the operation. But when the renal function improved the P values sank towards normal. The Ca and P values have remained normal during the postoperative observation period. Patient no. 2 has not been controlled because she left the country during the war, but we have heard that she has returned and is in good health.

In the case of hyperplasia the question as to permanent cure is more problematic. If too much of the gland is removed tetany with permanently low Ca values will result as in our patient no. 5.

However, the organism will gradually be adjusted to lower Ca values, and often there are no clinical symptoms of tetany in spite of subnormal Ca values. Still Ca should be administered in view to the danger of cataract (SALVESEN). During the acute stage of the tetany, *i. e.* the immediate postoperative period, the only effective treatment is large doses of CaCl, in some instances intravenously, because D<sub>2</sub> and AT 10 administration does not take effect until after a certain latent period.

If too little of the glandular tissue is removed, symptoms will persist as in the case of our patient no. 1, where only two glands were removed at the first operation. The Ca and P values returned to normal when the patient was re-operated. As previously stated, 30 to 300 mg glandular tissue should be left.

In the cases where the phosphatase values were increased, the values gradually returned to normal. However, it takes a longer time for the phosphatase values than for the Ca and P values to return to normal, this probably being a manifestation of the re-calcination following the operation.

In case 1 the phosphatase values remained high for several months after the operation.

### Summary.

The author reports 7 cases of hyperparathyroidism.

All cases presented typical findings in the blood, high Ca and low P values, except in one case where the P content was high as a result of an impaired renal function. The phosphatase values were increased in 3 cases. Six patients showed symptoms from the urinary tract and 5 from the osseous system. One patient had symptoms of an acute psychosis. At the operation 4 cases had an adenoma in the neck. In one patient no adenoma was found in the neck, but the patient was re-operated at another hospital, and an adenoma was found in the anterior mediastinum. Diffuse hyperplasia of the "water-clear cell" type was found in two cases. One of these patients had to be re-operated, because the glands on one side only were removed, the condition being interpreted as adenoma. No postoperative deaths occurred. In all patients with adenoma the Ca and P values returned to normal after the operation. Two patients had slight, transient symptoms of tetany. In one of two patients with hyperplasia the Ca and P values did not return to normal until the patient was re-operated.



In the other patient a permanent tetany developed because all parathyroid tissue in the neck was removed by a mistake. It is emphasized that the material seems to confirm the American dualistic concept, where adenoma and diffuse hyperplasia of the water-clear cells are differentiated. Frozen section should always be made at the operation. Should a water-clear cell hypertrophia be present, subtotal resection of the parathyroids should be done. In the case of adenoma it will suffice to remove this, because multiple adenomas are extremely rare. It is indicated that the term primary hyperparathyroidism may not be correct because the condition probably is secondary to a dysregulation of other endocrinous glands. If the so-called focal hyperplasia or adenoma really is a neoplasm, the term primary hyperparathyroidism seems justified.

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## On Surgically Treated Hepatitis.

By

STEN BRATTSTRÖM.

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In an interesting paper in *Acta Chir. Scandinav.* Vol. XCVI: 17: 1947, BERGENFELDT reports 7 surgically treated cases of acute hepatitis which were not ameliorated by a previous conservative treatment. The surgical treatment in BERGENFELDT's cases consisted of irrigation of the biliary passages with cholangiography contrast medium and saline solution, and resulted in a speedy regression of the icterus and the recovery of the patient. According to BERGENFELDT this favorable result was due to the perfusion's washing away an assumed mucus plug or an adhesion of the mucosa in the ductus choledochus which caused a relative obstruction of the biliary flow by the secretion pressure of the bile being lower than normal because of the primary hepatitic parenchymal process and thus not capable of removing the tenacious plug. The biliary stasis caused in this way by the mucus plug aggravated the hepatitis, and the vicious circle was first broken by the washing away of the plug.

In *Nord. Medicin* 1948: 38: 15 HUBLIN reports three cases of severe acute hepatitis and one of subchronic hepatitis in which two cases were treated with irrigation of the choledochus and the other two with irrigation and drainage of the choledochus. The three acute cases recovered entirely. HUBLIN's opinion with regard to the patho-physiological mechanism and the curative effect is in agreement with that of BERGENFELDT.

The theory originally set forth by VIRCHOW in 1865 that a stasis is present in hepatitis caused by a mucus plug in the ductus

choledochus has re-appeared and has been supported by observations made both in connection with the medical treatment of hepatitis with magnesium sulphate perfusions by means of a duodenal tube, where the mucus plug has been obtained before the biliary flow has commenced (MATSUO & MIZUTA, H. HULT), and in connection with surgical treatment, where choledochotomy in cases of hepatitis has revealed tenacious mucus, mucus plugs, or white bile in the distal portion of the choledochus. It is natural that the surgical principle of treatment should be to bring about drainage of the biliary passages by external or internal biliary fistulas, whether with a view to relieving some form of biliary stasis, producing drainage of a cholangitis, or drawing off infectious matter regurgitating into the biliary tree. Even if the motives have been divergent and the lines of reasoning not clear, it was early shown and has subsequently been confirmed by experience that external choledochus drainage in a considerable number of cases has been followed by regression of the icterus and the hepatitis.

Light seems to be shed on this fact by recent investigations, mainly in France, into the dystonias of the biliary passages and their significance. These are reported in excellent surveys in the *Journal de Chirurgie*, Tome 63, N:o 10—11, 1947. As these investigations will probably lead to significant consequences for the diagnosis as well as the therapeutic management of a number of obscure morbid conditions in the liver and the biliary passages, it seems justifiable to the author briefly to cite some of the main points in these papers, especially as they afford interesting points of view in the analysis of the present series.

By roentgen manometry, pharmacodynamic tests and physiologic stimuli there has in man been established a neuromuscular co-ordination of sphincter type at the neck of the gallbladder.

The bile from the liver accumulates between two obstructions, consisting of the sphincter of Oddi and the sphincter at the neck of the bladder. When the pressure is sufficient (10—14 cm. water), the sphincter at the neck of the gallbladder is relaxed and the gallbladder fills up. The filling and the relaxation of the sphincter may be blocked by a fatty meal or by morphine. The emptying is not a passive phenomenon and the sphincter at the neck of the bladder is a sluice lock which protects the choledochus pressure against excess pressure from the gallbladder.

The innervation of the neck of the bladder consists of an internal autonomous net of ganglia of Auerbach's type and an external

net connecting the region with the rest of the body by fibers which come through the lesser omentum from the plexus coeliacus and the vagus. The splanchnic nerve inhibits the muscle tonus in the biliary passages while the vagus accelerates it. These external nerves are not necessary for the function of the gallbladder. The bladder denervated from the external nerves still fills and empties, as shown by HOUSSAY and RUBIO. The fibers emanating from the vagus and splanchnicus exert only a regulating and restraining action, accelerating in the case of vagus and inhibiting in the case of splanchnicus, by acting on the internal autonomic nervous system. The nervous impulses over the vagus and splanchnicus are stimulated by the transduodenal passage of albumoses and peptones and by diluted hydrochloric acid which induces a motor reflex (according to IVY and GOLDBERG the hydrochloric acid should induce a hormonal reflex by liberating a "cholecystokinin" in the duodenum).

With regard to the choledochus, the presence of a triple sphincter system in the distal portion is stressed, namely: a papillary sphincter with circular, longitudinal and semicircular fibers, and a choledochus sphincter, about 15 mm. higher up, consisting of two segments, a lower corresponding to the choledochus situated intramurally in the duodenum and an upper a few millimeters higher up corresponding to the pars retroduodenalis choledochi. Here also the innervation consists of an internal autonomous net of ganglia of the Auerbach type and external fibers that connect it with the sympathetic and the parasympathetic system through the splanchnicus and vagus, respectively, enabling the sphincter of Oddi to act synergetically on the gallbladder and the sphincter of the neck of the bladder. The tonus-accelerating effect of the vagus and the tonus-inhibiting effect of the splanchnicus are identical in the bladder and the choledochus and its sphincter.

It is thus comprehensible that morbid processes and conditions of various types, even when at a considerable distance from the biliary passages, are able to disturb the delicately adjusted neuromuscular play in the biliary passages, causing dystonias there which give rise to manifest clinical symptoms. It has been possible to observe clinically the syndrome "atonia of the sphincter of Oddi" as it appears after sphincterotomy with its sequels: regurgitation, dilatation of the choledochus and cholangitis. Such observations, however, are exceptional. Commonly atonia of the sphincter occurs concomitantly with hepatitis. What correlation

is there then between the icterus and the atonia? The author cited, GUILLET, considers the icterus to be purely hepatocellular. He denies the possibility of its being sustained or even caused by the atonia with its sequels, regurgitation and infection, and adds that the hepatitis causes the dystonia, but without going into any further detail. He admits, however, that the condition calls for clarification, and he considers that the atonia of the sphincter plays an important rôle in the patho-physiological processes in protracted cases of hepatitis. It is, however, not only hypotonia that one encounters in connection with prolonged hepatitis and icterus, but also, as is shown by the roentgen manometric measurements, a hypertonia of the sphincter with an increase of pressure in the choledochus of more than 16—20 cm. water. This hypertonia may be purely functional and may temporarily yield to vagolytic measures, but it may also occasionally be conditioned by a true hypertrophy or sclerosis of the sphincter. What is then the correlation between the hypertonia and the icterus? A true retention icterus should imply a permanent excess pressure in the choledochus of more than 30 cm. water, and GUILLET seems to hold the opinion that the significance of the hypertonia lies in the relative stasis in the biliary passages, which sustains and aggravates the hepatitis and the hepatocellular icterus.

With the object of studying the significance of choledochus drainage in cases of prolonged hepatitis and problems related therewith, the author has made a survey of 14 cases admitted to the County and Municipal Hospital of Hälsingborg in the years from 1939 to 1947, inclusive, in *all* of which biopsies of the liver were done and in which the surgical therapy consisted of *external choledochus drainage* in all the cases but one (Case 9), where external choledocho-duodenostomy was performed according to PAUCHET. The cases are reported in the following and have necessarily been described rather summarily, wherefore some further explanation may perhaps be desirable. The *clinical diagnosis* of acute hepatitis has been made on the basis of the clinical course and the routine liver function tests, but the prolonged course, in many cases unimproved by medical treatment, or difficulties in differentiation, have indicated operation. In no instance has there been found any reason for the icterus condition other than more or less severe hepatitis. In two cases, however, there was microscopically demonstrated biliary stasis. In the three cases in which the pathologico-anatomical examination could not establish

hepatitis, no cause of the icterus could be discovered at all. In two of these cases (13 and 14) there were, however, increased phosphatase values and in the third case (12) there were increased phosphatase and citric acid values and a liver which on direct inspection suggested, "chronic hepatitis". In no instance did choledochotomy reveal mucus plugs, white bile, calculi, or anything similar.

The surgical procedure has consisted in careful exploration of the biliary passages with probe, scoop and palpation, and in an occasional case cholangiography also. Post-operatively the biliary flow has been collected by means of the choledochus drainage tube and measured, and in several cases it has been possible to show how the bile concentration has increased by permitting the drainage tube to empty into a bottle containing a certain amount of water and then testing the hemoglobin value of this mixture according to Autenrieth. The choledochus drainage tube has usually been removed after two weeks. All of the patients recovered or were improved in connection with the operation with the exception of one, who died on the 7th post-operative day in coma hepaticum and uremia. The thirteen surviving patients were later given follow-up examination.

The follow-up examinations have shown that 9 out of the 13 surviving patients are perfectly well. In two of these cases the period of observation is only four months, however. All of the cured patients showed normal values in the function tests. Of the three cases (7, 11 and 12) which did not show favorable late results, two have developed cirrhosis (7 and 11) and one (12) had a recidivation of the hepatitis after 6 months and was admitted to the medical department. Even upon operation the two cases of cirrhosis showed grave pathologico-anatomical changes, while upon biopsy the case of recidivation showed normal hepatic tissue but had a citric acid value in excess of 100 and a phosphatase value = 1.2 units.

## Case Reports.

The following abbreviations are employed: Bil = bilirubin in blood serum determined according to van den Bergh. Ci = citric acid in serum in  $\gamma$ /ml. Pho = phosphatase units per 100 ml. serum. PAD = pathologico-anatomical diagnosis of biopsy specimen of liver tissue.

*Case 1.* Female, aged 26. Painless icterus of 2 months standing, resistant to medical treatment. Referred from medical department. *Laboratory Findings* at operation: Bil 18/200000, Direct Reaction + + + +, Ci 62.1, Pho 5.6. *Operative Findings:* Gallbladder free from concrements or changes in the walls. Biliary passages normal, probed with ease. Liver surface found to be mottled with bluish-red elevated areas. *PAD:* Acute hepatitis with cellular infiltration. *Post-operative Course:* Post-operative attack of cholangitis. Otherwise steady regression of Bil to normal values. 2 months later renewed attack of icterus which abated slowly during sojourn in the medical department. *Follow-up Examination* 7 years later. Free from discomfort and symptoms since operation. Bil 2.25/200000, Ci 32.5, Pho 1.6, Takata neg.

*Case 2.* Female, aged 59. Painless icterus of 6 weeks standing, resistant to medical treatment. Bil 6.5/200000, Ci 38.1, Pho 16 at operation. *Operative Findings:* Gallbladder with solitary calculus. Brown-spotted, rather swollen liver. Biliary passages not remarkable. Cholangiography and choledochus probed, not remarkable. *PAD:* Hepatitic irritation with cellular infiltration in the portal connective tissue. Degenerative changes centrally in acini. *Post-operative Course:* Uncomplicated, decrease of bilirubin values to normal. *Follow-up Examination* 4 years later. Has been well. Takata neg., Ci 25.7, Pho 3, Bil 0.9/200000.

*Case 3.* Female, aged 53. Painless remittent icterus of 7 weeks standing, treated medically. *Laboratory Findings* 1 month prior to operation: Ci 39, Pho 17.6, Bil 8.6/200000, Direct Reaction + +. At operation: Bil 4.5/200000. *Operative Findings:* Gallbladder and biliary passages normal. Choledochus probed with ease. Liver swollen with rounded margin. *PAD:* Acute hepatitis with cellular infiltration of the portal connective tissue. *Post-operative Course:* Uncomplicated, with Bil falling to normal value. *Follow-up Examination* 3½ years after operation. Has been entirely well. Takata neg., Ci 25, Pho 3, Bil 0.9/200000, Galactose tolerance curve normal.

*Case 4.* Female, aged 56. 1½ years previously cholecystectomy and choledocholithotomy. Some months later and thereafter remittent attacks of icterus and symptoms of hepatitis. *Laboratory Findings* at operation: Bil 4.5/200000, Ci 27.5, Pho above 50. *Operative Findings:* Biliary passages normal, not dilated, no obstruction nor calculi. Liver yellow and swollen, hepatitis. *PAD:* Subacute hepatitis with proliferation of interstitial connective tissue. *Post-operative Course:* Uncomplicated, falling Bil, but still slightly icteric upon discharge. After 2 weeks the Ci was 21.9 and Pho 37.8. *Follow-up Examination* 3 years

after operation. Has been entirely healthy. Takata neg., Ci 23, Pho 26, Bil 1.4/200000.

*Case 5.* Female, aged 33. Diffuse abdominal and dyspeptic distress of two months standing, and icterus. Treated by medical department for 6 weeks prior to operation. *Laboratory Findings* 5 weeks prior to operation: Bil 25/200000, Direct Reaction ++, Ci 51, Pho 12, Takata neg. At operation: Bil 4.25/200000. *Operative Findings:* Gallbladder and biliary passages not remarkable, probed with ease. Liver thick and swollen with alternating light red and dark areas. *PAD:* Severe hepatitis, suggestive of *subacute yellow atrophy of the liver*. *Post-operative Course:* Uncomplicated. Bil values fell satisfactorily. Ci fell to 33, Pho rose to 17.8. Takata neg. Discharged well. *Follow-up Examination* 2 years after operation. Has been entirely well. Is working full time. Takata neg. Bil 1.1/200000, Ci 26.7, Pho 2.6, Galactose tolerance curve normal.

*Case 6.* Male, aged 51. Diffuse abdominal pain and icterus for 1 week. Cholecystography failed to reveal filling of gallbladder. *Laboratory Findings* at operation: Bil 4/200000, Ci 30, Pho 20.2, Galactose tolerance curve normal. *Operative Findings:* Gallbladder and biliary passages not remarkable. *Gallbladder compressed with ease.* From the biliary passages, which were probed with ease, bile obtained with a diastasic value of 1024 units. Liver not remarkable. Head of pancreas rather firm and thickened. *PAD:* Hepatitis. Biopsy from pancreas showed necrosis of fatty tissue. *Post-operative Course:* Uncomplicated. Bil fell to normal values, Ci rose to 32.7, Pho fell to 6, Galactose tolerance curve normal. Discharged cured. *Follow-up Examination* 2 years after operation. Entirely well. Working full time. Takata neg. Ci 22.8, Pho 2.6, Bil 0.75/200000, Galactose tolerance curve normal.

*Case 7.* Female, aged 56. Painless icterus of 4 months standing. Treatment in medical department without results. *Laboratory Findings* at operation: Bil 14.5/200000, Ci 39.3, Pho 26.8. *Operative Findings:* Gallbladder and biliary passages not remarkable. Bile ducts probed with ease. Liver swollen and firm, yellow-streaked with yellow spots — hepatitis. *PAD:* Subacute hepatitis. (11. 12. 1945.) Culture on bile gave growth of *b. subtilis*. *Post-operative Course:* Uncomplicated. Bil fell to 1.4/200000. Takata neg. Discharged improved after 7 weeks. Some days after discharge, increasing ascites. Readmission 1 month after discharge with ascites and distress from adhesions. *Operative Findings:* Laparotomy for relief of adhesions. Liver shrunken, hard and curved. Renewed *PAD* showed subchronic hepatitis. 11 months after initial operation, admission for post-operative hernia. Felt well, no ascites. Bil 2.20/200000. Upon operation for cicatricial hernia the liver was found to be shrunken and firm. *Biopsy* 5. 11. 1946 showed advanced changes, hepatic cirrhosis. *Follow-up Examination* 2 years after initial operation. Patient confined to bed with ascites and in need of frequent tapings.

*Case 8.* Male, aged 25. Painless icterus of 2 months standing, lassitude and fatigue. Treated in medical department. *Laboratory Findings*



at operation: Bil 18.25/200000, Ci 37, Pho 13.2. *Operative Findings:* Gallbladder and biliary passages not remarkable. Biliary ducts probed with ease. Liver swollen but otherwise normal. *PAD:* Hepatitis, abundant periportal and partially intra-acinous cellular infiltrations. Biopsy from choledochus normal. *Post-operative Course:* It was not possible to start the biliary flow from the choledochus drainage tube, and the patient died in the picture of coma hepaticum and uremia after 7 days.

*Case 9.* Female, aged 57. One year previously operated on for repeated unexplained attacks of pain in the upper abdomen. An explorative laparotomy with biopsy of the liver was performed. Nothing abnormal observed or palpated in the abdomen. Gallbladder rather large, easily compressed and without palpable calculi. Biopsy of liver showed normal picture. Ci 27, Pho 1.6. Present admission because of icterus of 2 months standing and intermittent attacks of pain in upper abdomen. *Laboratory Findings* at operation: Meulengracht 1:30, Ci 57, Pho 12.6. Takata + in 2 tubes. *Operative Findings:* Gallbladder and biliary passages not remarkable. Choledochus perhaps rather wide, probed with ease. Liver normal. Choledochoduodenostomia externa modi Pauchet was performed. *PAD:* Subacute hepatitis with tendency towards cirrhosis. *Postoperative Course:* Free from complications. Falling Bil to normal 0.5/200000, Takata neg. *Follow-up Examination* 1½ year after operation. Patient well, occasional abdominal discomfort, on one occasion probably attack of cholangitis. Takata neg. Bil 0.9/200000. Ci 25.7, Pho 4. Galactose tolerance curve normal.

*Case 10.* Male, aged 34. Icterus of 2 months standing. Treated in medical department for severe hepatitis. *Laboratory Findings* prior to operation: Bil 22.7/200000, Ci 34.2, Pho 8.8. Takata neg. *Operative Findings:* Gallbladder not dilated, biliary passages not remarkable. Yellowish edema in hepatoduodenal ligament. Liver enlarged and swollen. *PAD:* Hepatitis. Massive cellular infiltrations in the portal connective tissue and in the acini. *Post-operative Course:* Uncomplicated. Decrease in Bil, entirely well. *Follow-up Examination* 1 year and 4 months after operation. Patient entirely well. Has been under supervision. Bil 1/200000, Takata neg., Ci 53.4, Pho 0.6.

*Case 11.* Male, aged 61. Icterus and diffuse hepatic pains of 1 month's standing. *Laboratory Findings* prior to operation: Bil 9/200000. Direct Reaction ++, Ci above 100, Pho 11.2, Takata neg. *Operative Findings:* Gallbladder and biliary ducts not remarkable, probed with ease. Liver rather swollen, spotted and granular. Yellowish edema around the biliary ducts. *PAD:* Diffuse and chronic hepatitis with marked structural changes of the parenchyma. Culture on bile gave growth of species of pseudomonas. *Post-operative Course:* Uncomplicated. Fading icterus. Meulengracht's index: 1:18, Ci 27.5, Pho 9.8. *Follow-up Examination* 14 months after operation. Has felt tired and has had difficulty in working. No icterus, no dyspeptic distress. Palpation showed liver and spleen enlarged. Bil 1.25/200000, Ci 28.3, Pho 4, Takata pos. Referred to medical department.

*Case 12.* Female, aged 51. Remittent icterus of 10 weeks standing with attacks of pain, treated by physician. *Laboratory Findings* at operation: Bil 7.6/200000, Ci 34.2, Pho 17.4, Takata neg. *Operative Findings:* Gallbladder and biliary ducts not remarkable. Biliary passages probed with ease. Liver swollen, contour irregular, suggestive of chronic hepatitis. *PAD:* Bile stasis in liver. General structure of liver normal. No signs of hepatitis. Culture of bile gave *growth* of hemolytic streptococci. *Post-operative Course:* Uncomplicated. Bil fell to 0.85/200000. Discharge after 2 weeks. Ci 23, Pho 23. *Follow-up Examination* 6 months later. Patient admitted to medical department with renewed attack of icterus. Meulengracht 1:21, Ci 27, Pho 21.6, Takata neg.

*Case 13.* Female, aged 32. Cholecystectomy 2 years previously. Since then continued attacks of pain below the right costal margin and transitory slight icterus. *Laboratory Findings* at operation: Meulengracht 1:36, Ci 20.7, Pho 16.4. Takata neg. *Operative Findings:* Choledochus palpably widened. Probed with ease, however, and no calculi. *PAD:* Biliary stasis in liver. Moderate infiltration of inflammatory cells. *Post-operative Course:* Uncomplicated. Bil fell to 2.25/200000. Discharged well. *Follow-up Examination* 4 months after operation. Well, working full time. Bil 1.05/200000, Takata neg., Ci 28.7, Pho 2.2.

*Case 14.* Female, aged 53. 2 years and 9 months previously cholecystectomy + choledocholithotomy. Since that time remittent attacks of pain with slight icterus. *Laboratory Findings* at operation: Meulengracht 1:21, Ci 24.6, Pho 18.4, Takata neg. *Operative Findings:* Choledochus normal. Probed without difficulty. No calculi found. *PAD:* Normal liver parenchyma, but signs of bile stasis, dilated bile capillaries and bile plugs. Culture on bile: neg. *Post-operative Course:* Uncomplicated. Meulengracht 1:6, Ci 27, Pho 11.6. *Follow-up Examination* 4 months later. Free from discomfort, feels well, working full time. 2 months post-operatively Bil 1/200000, Takata neg., Ci 29.5 Pho 3.6.

### Discussion.

The series is small, but so are all series of surgically-treated hepatitis, as far as I have been able to ascertain. It may further be said that even cases of prolonged and severe hepatitis may spontaneously, apparently erratically recover after several months. Upon careful study of the present cases, it is difficult to avoid the impression that drainage of the choledochus had a close connection with the improvement and regression of the icterus which was obtained in all the cases except the one with a fatal issue. Even those cases that showed very serious microscopic parenchymal

changes improved, although in a few the later course and the follow-up examination showed that the improvement was temporary, and that one had to deal with progressing hepatic changes. On the other hand, at least four cases with serious microscopic parenchymal changes showed a genuine amelioration over periods of observation varying from 14 months to two years. It appears to the author that the results justify the surgical intervention in these cases, especially as, in addition to improvement, valuable information was obtained by the direct observation of the liver, the biliary ducts and the pancreas and the pathologico-anatomical examination of the biopsy specimens from the liver concerning the character of the disease.

*What*, then, is the significance of drainage of the choledochus in these hepatitis conditions? A conclusive answer to this important question can of course not be given on the basis of the present material, although it embraces at least five cases in which the history offers the combination of a previous cholecystectomy or remittent attacks of pain of biliary duct type, possibly with periods of icterus, suggesting some form of biliary dyskinesia or dystonia. It was pointed out above that French experimental studies have actually established the presence of such conditions of dystonia, and that the French research workers stress the relatively common incidence of such conditions in connection with cases of "*ictère médicale prolongée*", *i.e.* hepatitis, whatever the correlation may be.

If one accepts the incidence of such conditions of dystonia and acknowledges their significance in certain hepatic conditions, either as causing or contributing to the pathogenesis of the hepatitis or as aggravating or prolonging its course, it seems understandable that drainage of the choledochus should have a beneficial effect, whether there is question of a hypotonia in the sphincter apparatus with a regurgitating infection or of a condition of hypertonia with a relative bile stasis and its unfavourable effect on a hepatitis process.

It is to be hoped, and we have reason to expect, that continued cholangiographic and manometric studies of these conditions will throw light on these relationships and lead to results of practical importance. If we could arrive at the point where we had some convenient means of forming an opinion during actual operation concerning possible disturbances in tonus and pressure in the biliary ducts, it might be practicable to supplement the temporary good results of drainage of the choledochus with additional surgical

measures in the form of vagotomy or splanchnicotomy, possibly in association with sphincterotomy, aiming at a causal therapy of lasting effect.

As a matter of fact, reports have already been made of such interventions on these indications. MALLET-GUY (2) has presented a small series of such cases in which the effect has been satisfactory and lasting.

*In summary*, it may be said:

that in obscure prolonged cases of hepatitis, it is important to bear in mind the great significance of the dystonias of the biliary passages;

that these biliary passage dystonias are in many cases amenable to surgical procedure, and that therefore conservative medical treatment should not be pursued interminably, perhaps with disastrous consequences to the liver parenchyma;

that a more accurate knowledge of the physiology of the biliary passages, combined with continued manometric and cholangiographic studies during operation, should afford a sound basis for surgical intervention involving the vagus, the splanchnicus or the sphincter of Oddi, and that the experiences already gained speak in favour of our arriving hereby at a causal therapy;

that pending greater experience with the measures mentioned above, we have in external choledochus drainage a procedure which combines a low incidence of risk with an undoubtedly beneficial effect on the hepatitis, whether this effect be temporary or, as is occasionally seen, lasting.

### Summary.

The author cites earlier literature on cases of acute hepatitis with a prolonged course which were surgically treated by means of perfusion of the biliary passages with good results. The beneficial effect has been ascribed to the washing away of an assumed mucus plug in the choledochus which constituted a relative obstruction to the biliary flow when secretion pressure was lowered by primary hepatitis. In this connection, a brief account is given of recent French studies on the physiology and patho-physiology of the biliary passages, studied by means of cholangiography and manometric measurements during operation. The authors of these studies have considered themselves able to show that a condition of dystonia within the biliary passages or disturbances of the

neuromuscular co-ordination in the sphincter system play an important rôle in the origin and course of certain acute prolonged hepatitic conditions. Experience suggests that a closer analysis of the dystonias by means of cholangiography and manometric measurements of pressure conditions during operation would facilitate a rational surgical therapy in certain conditions of hepatitis by indicating vagotomy, splanchnicotomy or sphincterotomy. Experience already gained in this field affords further clarification of the beneficial effect, long recognized in several quarters of external choledochus drainage. From the Surgical Department of Hälsingborg's County and Municipal Hospital the author reports 14 cases in which the clinical diagnosis was acute hepatitis and the surgical procedure consisted of drainage of the choledochus.

In all of the cases, biopsy of the liver was done at operation, and the 13 surviving cases were re-examined. In 13 cases intervention resulted in immediate improvement, although in several instances there were serious microscopical changes and the biopsies revealed parenchymal lesions. 2 cases subsequently developed cirrhosis and after a lapse of 6 months one had a recidivation of the hepatitis.

The author stresses the great importance of the dystonias of the biliary passages in certain obscure prolonged cases of hepatitis and points out that in many instances these are amenable to surgical treatment and that a conservative therapy should not be pursued unduly long, as disastrous effects on the liver parenchyma may ensue.

Cholangiographic and manometric studies during operation may on careful analysis afford indications for intervention involving the vagus, the splanchnicus or the sphincter of Oddi. Pending further experience of these measures, we have in external choledochus drainage a fairly safe procedure which undoubtedly has a beneficial effect on the hepatitis process.

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## Pyelo-Uretero-Cystitis Granularis Sive Cystica.

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Cystic formations of the urinary tract is a rather rare condition. MORGAGNI, in 1822, was probably the first who described the disease. At autopsy LUBARSCH found 4 cases in 3,000, and WILSON 2 in 5,000. According to WILSON, 70 cases had been published prior to 1934.

The cysts may be situated in the bladder, ureteres, or renal pelvis, but are most commonly found in the bladder or in the lower part of the ureteres. They appear as pearls of dew on the mucous membrane, the size varying from that of a pinhead to that of a pea. The contents may be clear, yellowish, or brownish. Often the cysts are filled with a yellowish brown, tenacious fluid. Miliary nodules and discoloring of the mucous membrane caused by the healing of bursted cysts may be seen. The wall may become fibrously thickened and stiff.

Many publications exist where attempts have been made to explain the formation of the cyst. Some of these publications which are referred to, I know from reports only. Most authors apparently hold that the formation of cysts is a result of a chronic inflammation of the urinary tract (HERXHEIMER, ASCHOFF, MORSE, and GIANI). The long-continued chronic inflammation causes new formation of epithelium which grows into the submucosa. These epithelial islands degenerate, thus forming cysts which penetrate to the surface where they may burst and give rise to hemorrhage. Another way in which cysts may be formed is that

the lacunae normally present become clogged by granulation tissue. This is considered as a common mode of formation at the neck of the bladder where there are many lacunae (SALTYKOW, JACOBSON). Common for both views is that the inflammation is considered as the main cause of the cyst formation.

The symptoms which may occur depend on the number, size, and location of the cysts. Few and small cysts may not give any symptoms, especially those situated in the bladder. But large and numerous cysts of the ureteres or renal pelvis may cause obstruction to the outflow of urine.

In typical cases where the lesions are located to the bladder, the condition is easily diagnosed cystoscopically. If the cysts are located to the ureteres and renal pelvis only, the diagnosis may be difficult and can only be made by roentgen examination. Minor defects are easily overlooked as the ureteres are often poorly filled as well by the usual urography as by pyelography, and because the condition is so rare and little known.

The following case might be of interest, as it appears that the condition ought to be considered in obscure cases of hematuria, and because it shows that the roentgen examination under favourable conditions may lead to the goal even if the cystoscopical findings give no clue to the diagnosis. The case also shows that the disease in this patient has no healing tendency even if the infection is treated, as previously believed. The case has been followed for  $4\frac{1}{2}$  years by repeated control examinations. The past history is just briefly mentioned.

The patient is a woman, aged 48, who was admitted to the Surgical Département on April 22nd, 1942, for a hematuria which was accidentally diagnosed one month previously. There had been no frequent or painful micturition, no fever. S. R. 16 mm. Urine: Smoky, albumin +, blood +, pus +.

*Urography, March 24th, 1942:* The renal shadow measures 11 by 5.5 cm on the right side, 14 by 6.6 cm on the left. The excretion is somewhat retarded on the right side, and the lower calices are rather unsharply outlined. The renal pelvis on both side are of the same size. The medial contour of the lower part of the left ureter has a small, round, smooth defect of the size of half a pea (fig. 1 and 2).

*The diagnosis was:* small right kidney with unsharply defined lower calices on the right side.

On April 27th, 1942, *cystoscopy and ureteral catheterization* was performed. The ureteral openings were somewhat narrower than usual. Slightly cloudy urine was obtained from the left side. There was no obstruction to the passage of the catheter. On the right side the catheter stopped 5 cm above the ureteral opening, and only sparse

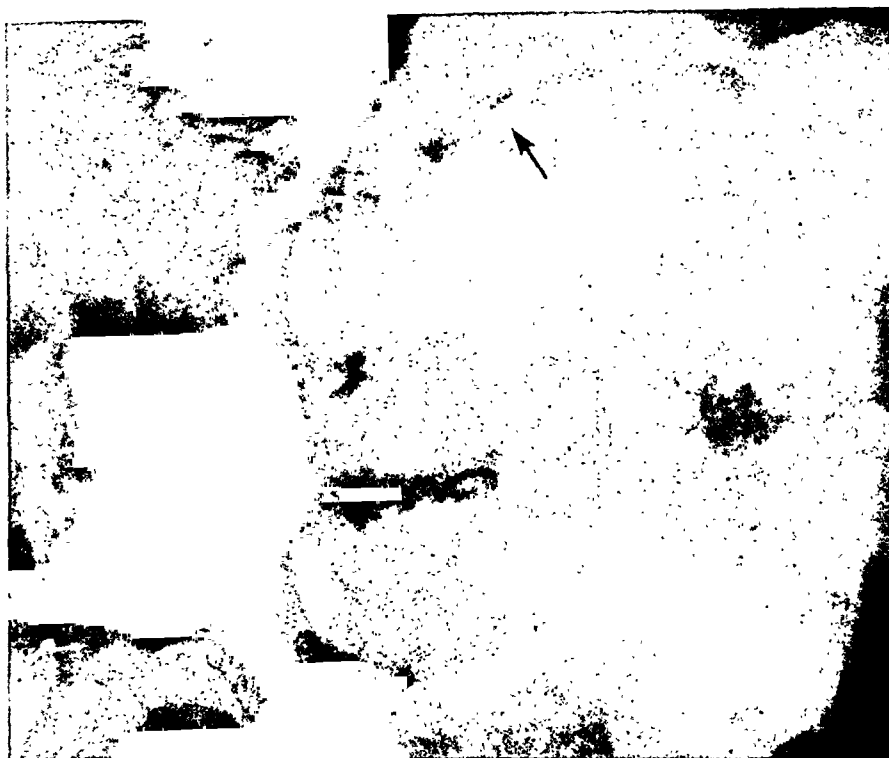


Fig. 2. Defect in the lower part of the left ureter.



Fig. 1. Renal pelves of same size. Defects in both ureters.

SKOGSTAD: Pyelo-Uretero-Cystitis Granularis Sive Cystica.





Fig. 4. Numerous matchhead-sized defects in both ureters.

Fig. 3. Defects in the right renal pelvis and upper part of the ureter.

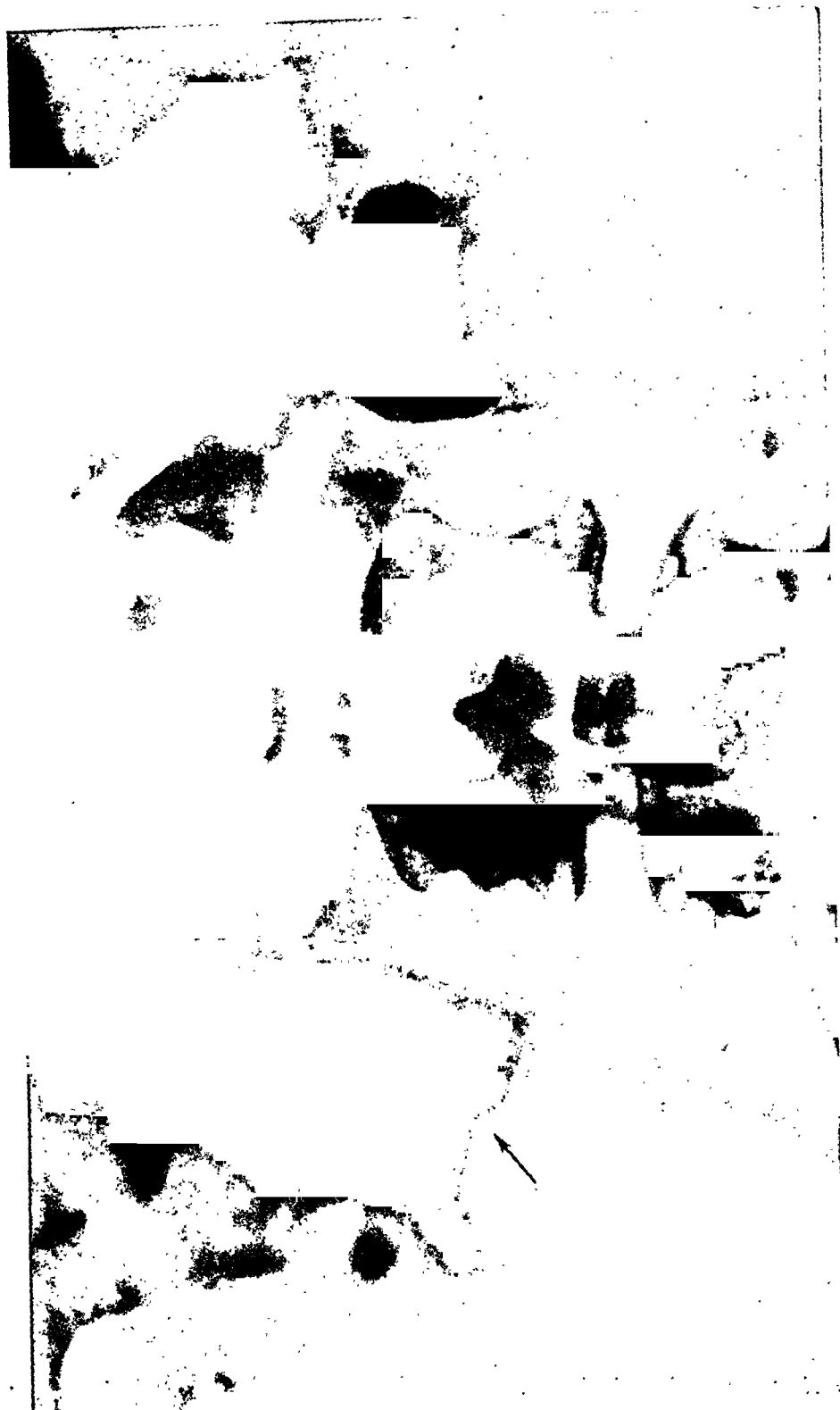


Fig. 5. Four years later. The right renal pelvis and calices are enlarged. The right ureter is dilated and shows small defects.

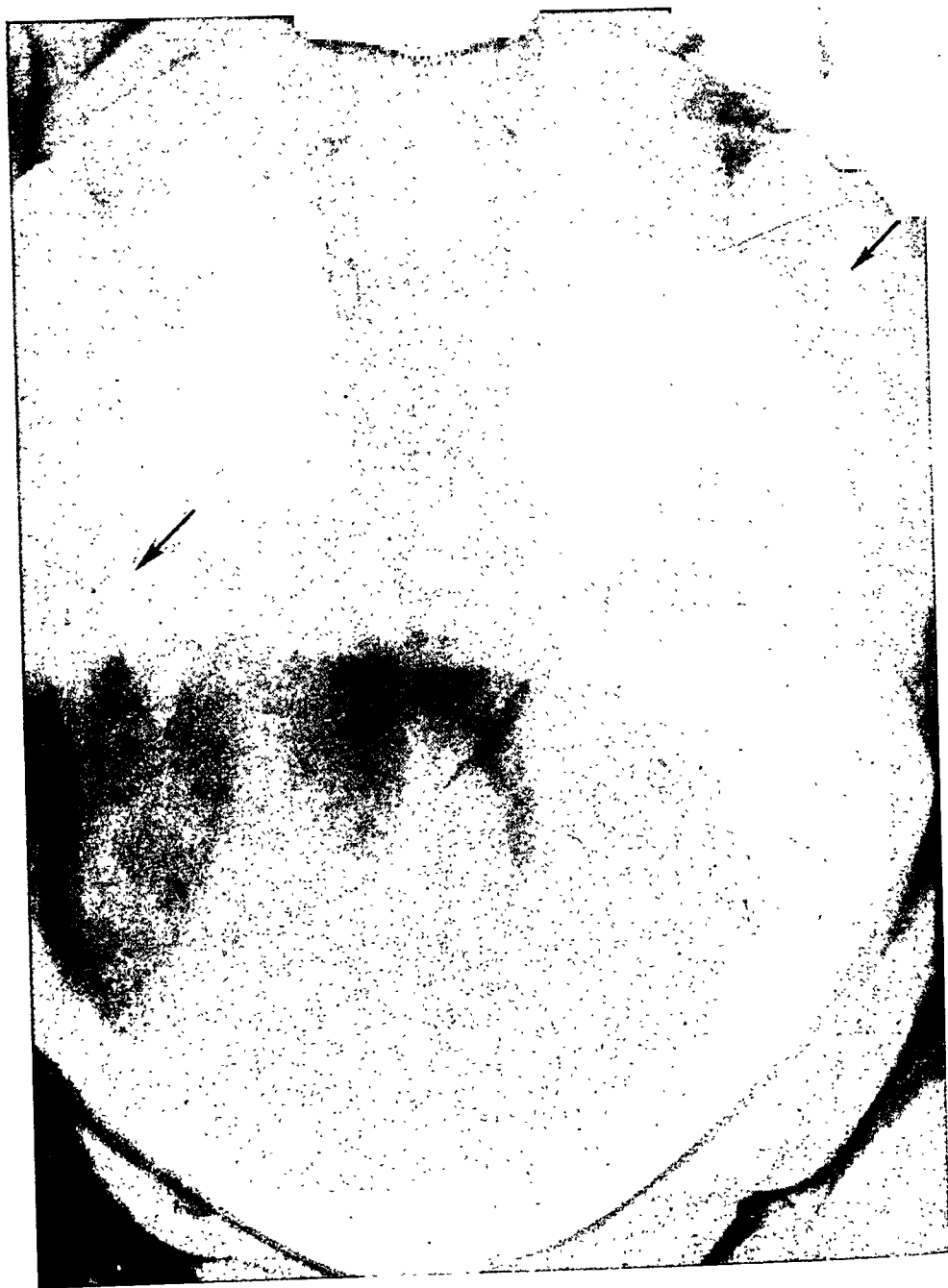


Fig. 6. Numerous defects in both ureteres and obstruction to the outflow of urine.

amounts of urine could be obtained. Both specimens contained numerous red blood cells, only few white cells. The bladder mucosa was normal, and so was the bladder capacity.

Hematuria persisted during the hospitalization. The patient was discharged to wait for the result of cultivation on Hohn's medium, but this was negative.

The patient was then readmitted on June 22nd, 1942, for repeated examination, *cystoscopy* and *pyelography*. Also this time the bladder mucosa was normal except for some varicous veins which did not bleed. From the right side almost clear urine was obtained, but that from the left contained blood. *Retrograde pyelography* with 10 per cent abrodil (no air in the syringe, dripping catheter) revealed a couple of matchhead-sized, round defects in the lower part of the right renal pelvis and in the upper part of the right ureter. A pyelo-ureteritis cystica was then being suspected, and by reviewing the urograms taken on April 22nd, additional areas of rarefaction were found. R: Pyelo-ureteritis cystica (fig. 3).

The patient had also during this hospitalization bloody urine. So she also had for the last two weeks prior to the admission on August 10th, 1942, although the urine was negative during this hospitalization. The *urography* revealed the same findings as on the previous examinations (fig. 4).

*Cystoscopy* repeated on December 30th, 1942: At the neck and posterior parts of the bladder some pinhead-sized yellowish spots are seen on a congested mucous membrane. A little further above and to the left, some similar spots are seen, but here the bladder mucosa is normal. The left external opening of the ureter is surrounded by a swollen mucosa which just above the opening is bulging over a bluish underlying structure. The right part of the bladder is not involved, and the ureteral opening is normal. The aforementioned yellow spots seem to be confined to the vessels, being situated on or along these. No ulcerations could be seen in the bladder.

Since 1942 till December 5th, 1946, the patient has suffered repeated attacks of hematuria, but this has never been associated with painful micturition. The hematuria has each time persisted from one to several weeks. She has received periodical treatment with different urinary disinfectants, but the pyuria and hematuria have always relapsed. Her general condition has not been affected, and it was only on account of the hematuria that she consulted a physician.

*Urography* repeated on December 5th, 1946, showed that the excretion on the right side was considerably reduced. The renal pelvis is somewhat enlarged. The calices are sharply defined on both sides. The lower boundaries of both renal pelves present small, round areas of rarefaction. The right ureter is somewhat dilated, and in both ureters there are several small areas of rarefaction. Especially the contours of the lower parts of the ureters are uneven and unsharply defined on account of these defects. There is apparently some obstruction to the outflow of urine, both ureters being filled with contrast in their lower parts (fig. 5 and 6).

### Summary.

In a 48-year-old woman an ureteral hematuria was diagnosed, the hematuria having persisted for periods during the last  $4\frac{1}{2}$  years. Her general condition has been good all the time, no dysuria. The sedimentation rate was on several occasions 15—16 mm, urea 45 mg pr 100 cc. Tubercle bacilli could not be cultivated from the urine. Urography and retrograde pyelography revealed findings typical for a pyelo-ureteritis cystica, but this was not found at cystoscopy, which, however, seemed to confirm the diagnosis on the last examination. No permanent cure could be obtained by treatment with urinary disinfectants, and after  $4\frac{1}{2}$  years the cyst formation has increased so that the condition represents a moderate obstruction to the outflow of urine, the pelvi-vesical tract on the right side being dilated, and the excretion of contrast being impaired on this side.

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From the Surgical Clinic, Lund, Sweden.  
(Head: Prof. J. P. STRÖMBECK)

## Hemorrhoids and Cancer.

By

NILS CARSTAM.

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The term "hemorrhoids" may be said to designate an enlarged and varicose condition of the hemorrhoidal veins. Hemorrhoids are divided substantially into two classes, first, external hemorrhoids, which arise in connection with the venous plexus pertinent to the inf. hem. vein belonging to the caval system, and which are located below the ano-rectal junction and covered with the skin of the anus; and secondly, internal hemorrhoids, which arise in connection with the venous plexus pertinent to the sup. hem. vein belonging to the portal system, and develop in the terminal branches of this plexus, in the columns of Morgagni, and are covered with rectal mucosa. These two types of hemorrhoids are often co-existent and sometimes merge into one another, in which case they are known as interno-external hemorrhoids. External hemorrhoids are relatively less serious and less important, but may, however, involve complications such as infection and anal hematoma, which in turn may give rise to painful conditions necessitating treatment. Bleeding is a less common accompaniment of this type of hemorrhoids.

Owing to their symptomatology, in which bleeding is the predominant symptom of uncomplicated cases, internal hemorrhoids constitute the more serious and important type, not only because of the pain and discomfort they give and the troublesome conditions they cause, but also because their recognition is of valuable differential diagnostical significance in establishing the diagnosis of other rectal lesions. From now on in this paper the term "hemorrhoids" is understood to comprise internal hemorrhoids only.

Hemorrhoids are most common in middle-aged people but are also a frequent occurrence in elderly and even very old persons. Furthermore hemorrhoids are encountered more often in males than in females, the generally accepted ratio being about 1.5—2 : 1. At any rate hemorrhoids are an extremely common lesion and it has been said that almost everybody at some time or other has symptoms ascribable to hemorrhoids. Such assumptions and assertions are, however, hard to evaluate, and do not lend themselves to comparison owing to relatively different bases of calculation, for instance, a study of the frequency of hemorrhoids calculated on the basis of trouble and *symptoms* suggestive of this lesion will differ from the results of a study of the incidence of *clearly established* hemorrhoids. Even in the last mentioned case it is sometimes hard to decide what is normal and what is pathological as all sorts of intermediate stages are encountered, from a normal venous plexus to distinctly pathological varicose changes of considerable magnitude. Furthermore the incidence probably varies in different classes of people with different ways of living as well as in different climates and different races.

Hemorrhoids were described already early in history. Even HIPPOCRATES suggested operative methods and recommended the use of a speculum for rectal examination, which method was forgotten during the middle ages — and is often ignored even today. Already far back voices were raised warning against confusion of hemorrhoids and rectal cancer, the Dutchman RUYSCH emphasizing this danger about the year 1700 when he described the pathology of cancer of the rectum, but the difference between hemorrhoids and rectal cancer was not generally recognized until the beginning of the nineteenth century when BAYLE published a description of the clinical picture of this type of cancer.

In the latter part of the nineteenth century during the actual development of surgical therapy of rectal cancer attention was paid to the question hemorrhoids—cancer, hemorrhoids being considered an etiological factor of cancer. VOLKMANN contends "dass es besonders Leute, die schon Decennien an Hämorrhoidalbeschwerden und chronischem Katarrh des Rectums, an Obstipation leiden, sind, bei denen es zu einer Neubildung kommt". In most of the statistics available on rectal cancer dating from this time and from the beginning of the twentieth century the frequency of hemorrhoids is also given, *e. g.*, LÖVINSOHN evaluates it to be 25.9 per cent, STIERLIN 15 p. c., CSESCH 7.3 p. c.; SUTER

9.5 p. c., ZINNER 11 p. c. None of these numbers are based on objective findings but founded on anamnestic data or obtained from information available from routine records. Also later authors have dwelt on this problem, such as D. F. JONES, HAYDEN and SHEDDEN, but as a rule they do not believe in the existence of any etiological relationship, first, because cancer seldom arises in hemorrhoidal sites, and, secondly, because the occurrence of hemorrhoids is so extensive that the arising of cancer in the area of pre-existent hemorrhoids must be considered a pure coincidence.

Many authors consider hemorrhoids a symptom of rectal cancer. In 1907 LOCKHART MUMMERY said that the appearance of hemorrhoids in elderly persons is often due to rectal cancer, and that he has seen many such cases in which cancer had not been discovered at operation for hemorrhoids. Other authors have pointed out how difficult it is to distinguish hemorrhoidal symptoms from those suggestive of cancer, and contended the frequent co-existence of these two lesions without, however, endeavouring to give an explanation why this should be so. For instance, figures obtained from Mayo Clinic have been published according to which 10—20 per cent of the patients admitted to the Clinic for rectal cancer had on account of rectal bleedings been operated on for hemorrhoids shortly before hospitalization, a further percentage having been treated in some manner or other for hemorrhoids by private practitioners who did not detect cancer. Similar figures, 10—65 per cent, have been published by other authors such as JONES, HAYDEN & SHEDDEN, YEOMANS, and RANKIN.

Besides this, many patients with rectal bleedings or other symptoms suggestive of cancer believed that they had hemorrhoids and therefore did not trouble to seek medical aid before the appearance of other symptoms, by which time the cancer had often become inoperable.

The serious result of such delay has, above all in U. S. A., been brought to the notice of the medical world, especially practitioners, it being urged to palpate, and to perform a rectoscopic and possibly roentgenologic examination of the rectum of patients with hemorrhoids and other apparently innocent lesions. BUIE says "it should be strongly urged that all patients who have symptoms referable to the rectal outlet be considered to have carcinoma until it is proved that such a lesion does not exist".

In his introductory lecture held before the Nordisk Kir. Förening, 1933, SÖDERLUND said that he believed hemorrhoids to be a symp-



tom of cancer of the colon and when this was the case, most frequently of sigmoidal cancer. Two patients in his series consisting of 152 cases had been operated on for hemorrhoids prior to hospitalization. He therefore recommends a roentgenographic examination of the colon in all cases of hemorrhoids in patients in cancer ages. CRAFOORD, who also met with a similar case, likewise urges that such patients be roentgenologically examined.

As soon as rectal cancer is suspected in patients at the Surgical Clinic, Lund, they are as a rule naturally examined by palpation, often complemented by rectoscopy and sometimes by biopsy. The colon is as a rule X-rayed in order to exclude the co-existence of cancer further up the colon or to determine the upper border of the tumour and possibly the length of the sigmoid flexure, but this radiographic examination plays no part in the establishment of the diagnosis "rectal cancer".

In the establishment of cancer of the colon, however, the roentgenologic examination is of quite a different diagnostic significance. In such cases the clinical behaviour of the lesion gives rise to the suspicion and the diagnosis is verified by the radiographic examination. The radiographic examination is generally performed with the aid of opaque enema, sometimes combined with the passage of an oral meal if changes in the ilio-caecal region are suspected.

Since 1940, not only a thorough palpation of the rectum but also a roentgenologic examination of all cases of hemorrhoids in patients over 40 yrs. of age has been the rule at the Surgical Clinic, Lund. On an average about fifty such X-ray examinations were performed annually; this number was of necessity somewhat smaller during the latter part of the war.

The admission cards of those patients who were registered as colonic cancer cases subsequent to roentgenologic examination during the years 1940—46 have been scrutinized. Many of the cards had however not been filled up properly or contained insufficient data and therefore cannot be considered reliable. In doubtful cases attempts were made to complete the data by reference to the records, which was as a rule possible because the patient was generally an inmate at the time of the radiographic examination or was admitted immediately thereafter. The reasons why X-ray examinations were deemed necessary have been roughly divided into groups, apparent from the following table.

*Indications for Roentgenologic Examination of 164 Cases of Cancer of the Colon.*

	1940	1941	1942	1943	1944	1945	1946	Total
I. Hemorrhoids without other symptoms (Routine examinations) .....	—	—	—	—	—	—	—	—
II. Suspicion of tumours general symptoms, obstipation etc. with bleeding as a partial symptom	2	6	12	5	11	6	1	43
III. Suspicion of tumour, obstipation, palpable abdominal tumour etc. without bleeding...	12	8	9	16	9	8	15	77
IV. Symptoms of colitis, intestinal obstruction .....	4	3	14	1	1	5	9	37
V. Palpable tumour per rectum ..	1	—	2	—	1	—	2	6
VI. Reason untraceable .....				1				1
								164

The routine examination of patients with hemorrhoids but without other symptoms has thus not led to the discovery of cancer of the colon in any of the cases of the above material.

In the present study the author has endeavoured to determine the frequency and correlation between hemorrhoids and cancer of the colon and rectum. Cases of cancer of the colon and rectum were examined to ascertain the presence or absence of hemorrhoids a similar examination being made on control material.

The above examination was carried out in the following manner. The day after admittance or as soon as the diagnosis had been established anoscopic examinations were performed without the previous administration of laxatives or enema, the patient lying on his left side. Use was made of a short anoscope, illuminated by means of a pocket torch. The obturator was removed after the introduction of the anoscope, which was then slowly withdrawn during which the lower part of the rectal mucosa and the ano-rectal junction were inspected and the existence and location of possible hemorrhoids registered on a diagram. The examination was then repeated, during which the pat. was requested to strain down. The examination was completed by palpation. Palpation alone is however insufficient to establish the existence of hemorrhoids because uncomplicated hemorrhoids are as a rule unappreciable by touch. The anoscopic examination does not always enable one to conclude the presence or absence of hemorrhoids because, as mentioned above, the drawing of a line between

normal, and pathological conditions is a question of experience. Due heed should, however, be paid to the degree and extension of possible changes, especially with regard to unchanged remnants of the columnae rectales in cases with but one or two nodules, and to the colour and nature of the mucosa. This of course makes it difficult to determine the absolute frequency of hemorrhoids, but it is compensated when comparisons are made with control material, provided that all the examinations are performed by one and the same examiner and under identical conditions, as was the case in the present study.

### Cancer Material.

In the course of eighteen months (1946—47) 51 cases of rectal cancer admitted to the Surgical Clinic were examined. Of this number 29 were colonic and 22 rectal cases. The rectal cases were collected during a relatively shorter time than the colonic cases because the purpose of the present investigation was initially limited to colonic cancer only, so that the numerical relationship in this paper between these two sorts of cancer is not illustrative of the true relative proportion, but this is of no importance as far as the present study is concerned.

The age- and sex incidence will be apparent from the following table:

Age	Yrs.	30—39	40—49	50—59	60—69	70—79	>80	Total
Males .....		1	3	4	6	15	2	31
Females .....		1	4	2	7	6		20
Total		2	7	6	13	21	2	51

The above numbers agree rather well with the statistical values of colonic and rectal cancer published, for example, by DUKES, RAIFORD, BIEREN, JOHNSON and COLCOCK, but the average age is higher than that in the material of most other writers.

### Control Material.

In order to obtain an idea of the incidence of hemorrhoids in corresponding age-groups, examinations were performed on a control material consisting of patients admitted to the surgical

and orthopedic departments. Patients of a suitable age and without counter-indications, were examined the day after their admittance under the same conditions as the cancer material. For practical purposes acute illnesses or fever prohibiting the removal of the patient for examination, or admittance for hemorrhoids or other intestinal lesions as well as abdominal trouble, and such diseases as are considered to favour the arisal of hemorrhoids *e. g.* hypertrophic prostate, abdominal or pelvic tumours etc. were considered to be counter-indications. So that the control material might not be influenced by the inclusion of patients with a possibly general weakness of the venous system and predisposition for varices, cases with varices or varicose ulcers of the leg were likewise excluded.

*Age- and Sex Incidence.*

	Yrs.	30—39	40—49	50—59	60—69	70—79	>80	Total
Males .....		1	4	13	16	12	3	49
Females.....		2	5	15	20	13		55
Total		3	9	28	36	25	3	104

The number of cases of hemorrhoids demonstrable in the cancer material and in the controls will be apparent from the following table.

	Nr. of cases	Occurrence of hemorrhoids	
		Nr.	Per cent.
Cancer material .....	51	19	37
colonic .....	29	13	45
rectal .....	22	6	27
Control material.....	104	43	41

These numbers are of course too small to be conclusive but nevertheless they do argue against the assumption that hemorrhoids are more common in patients with colonic or rectal cancer than in otherwise healthy people.

The location of the tumours and the number and location of those with pos. hemorrhoidal findings is shown in the following table:

Localization	Nr. of cases	Hemorrhoids
Cecum + ascendens .....	5	2
Transversum .....	1	1
Descendens .....	6	3
Sigmoideum .....	17	7
Oral portion .....	(8)	(3)
Rectosigmoid .....	(9)	(4)
Rectum .....	22	6
Located with lower border $\geq$ 5 cm fr. anus ..	(18)	(5)
Located with lower border $<$ 5 cm fr. anus ..	(4)	(1)

Hemorrhoids have been considered by some authors to be a symptom of cancer of the lower colon and rectum. The mechanism of its arisal in such cases is believed to be a stasis in the sup. hem. plexus due either to a direct overgrowth and pressure on the draining veins in the rectal wall or on the actual venous trunks after they have pierced the rectal wall and continue upwards to the inferior mesenteric vein. This mechanism can thus apply only to tumours in the rectum and the rectal sigmoid and possibly, if pressure is exercised by glandular metastases and such pressure be of any significance, possibly also to tumours in the rest of the sigmoid and the colon descendens.

If we consider the cases in the light of the above and class them accordingly, the results will be as follows.

	Nr. of cases	Nr. thereof with hem.
Colon, except rectosigm. ....	20	9
Rectosigmoideum and rectum. ....	31	10
Total	51	19

or

	Nr. of cases	Nr. thereof with hem.
Right colon (caecum, ascendens, transversum) ..	6	3
Left colon (descendens, sigmoid, rectum) .....	45	16
Total	51	19

These tables do not argue for such arisal mechanism because cases with tumours within the drainage area of the inf. mesenteric vein exhibit a lower hemorrhoidal frequency than cases with tumours in the other part of the colon, and in the present study even lower than that in normal material. Neither has it been possible to ascertain any definite relationship between the location

of hemorrhoids and the topical location of the tumour in cases of rectal cancer. A common arrangement of the principal columns affected by hemorrhoids is: left lateral, right anterior, and right posterior, this arrangement being explained by the fact that the sup. hem. artery is divided into two main branches, the left passing down the wall undivided, the right however dividing into anterior and posterior branches. One might be inclined to expect hemorrhoidal affections of one or more of these columns depending on the site of the cancer, but in the few cases of the present material in which hemorrhoids could be shown no such relationship was establishable.

As mentioned further up, most of the literature available on the co-existence of hemorrhoids in cancerous patients refer to hemorrhoidal symptoms or anamnestic reports on the treatment of, or operation for, hemorrhoids. Of these 51 cases none had been operated on for hemorrhoids within a few years previous to admittance and only one patient had sought relief for hemorrhoids prior to hospitalization. One of the reasons for the difference between this material and reports originating from U. S. A. according to which 10—65 per cent of hospitalized cases of rectal cancer had been treated for hemorrhoids a relatively short time before admittance to hospital may possibly be attributed inter alia to the fact that in Sweden practically all operations for hemorrhoids are performed at public hospitals where it is easier to examine doubtful cases.

At examination both the cancer patients and the controls were asked whether they had or thought they had hemorrhoids and whether they had noticed any bleeding during defecation, or blood streaks in their stool.

Of the 19 cases of cancer in which the co-existence of hemorrhoids could be established 12 patients said that they believed they had hemorrhoids, and 13 patients said that they had observed fresh bleedings in some form or other from the anus during the last two years.

Cancer cases in which hemorrhoids were demonstrable:

	Nr.	Hem. subj.	Bleeding.
Colonic cancer .....	13	8	8
Rectal cancer .....	6	4	5
Total	19	12	13

Of the other 32 cases of cancer in which the examination did not disclose the existence of hemorrhoids, the answers to the above questions were as follows:

Cancer cases in which hemorrhoids could not be shown:

	Nr.	Hem. subj.	Bleeding
Colonic Cancer .....	16	5	6
Rectal Cancer .....	16	4	12
Total	32	9	18

A similar questioning of the controls gave the following result:

	Nr.	Hem. subj.	Bleeding
Cases in which hem. could be demonstrated. ....	43	22	13
Cases in which hem. could not be demonstrated. ....	61	16	7

In many cases in which hemorrhoids (internal) could not be discerned, but in which the patient believed to suffer from them, external hemorrhoids or hemorrhoidal remnants were observable. The reason why the findings did not always agree with what the patient said may, to a certain extent, be due to the fact that patients use the term hemorrhoids as a general name for any sort of trouble in the anal tract, and thus at times for symptoms suggestive of cancer. In several cases of the control material slight anal fissures were observable, which may explain why in some cases the patients had noticed bleedings in spite of the absence of hemorrhoids.

The number of macroscopic bleedings reported — 45 p. c. for colonic cancer and 77 p. c. for rectal — agrees well with the percentage found, for example, by GABRIEL, DIXON, RANKIN & GRAHAM, JOHNSON, the number 45 p. c. for cancer of the colon is however somewhat high. This may be explained by the fact that the present material includes those cases with but a very slight bleeding in conjunction with hemorrhoids, which was possibly neglected or not taken into account in other statistics.

Thus, although this study is not conclusive of any etiological relationship between hemorrhoids and cancer, it does show how common the co-existence of hemorrhoids and cancer really

is, the liability to overlook cancer in patients with hemorrhoids being obvious, unless an examination is made further up the large bowel, which by general assent, ought to consist of a thorough palpation, complemented by rectoscopy and sigmoidoscopy, whereby it is possible to diagnose 75—80 per cent of cancers of the large bowel, which is the proportion of cancer encountered in the rectum and the recto-sigmoid (T. E. JONES).

The frequency of hemorrhoids seems to be just as great in cases of cancer in the remaining part of the colon as in patients with recto-sigmoidal cancer but in the latter cases the liability to confusion is not so great. A tumour located superior to the recto-sigmoid and consequently not visible through the sigmoidoscope, but which gives a fresh bleeding is probably of a more advanced degree and has presumably given rise to other symptoms that might be suggestive of a tumour of the colon and render a radiographic examination advisable. If on the other hand anoscopy of a patient free of symptoms of a tumour permits a clear diagnosis of hemorrhoids, and palpation and sigmoidoscopy permit one to establish the absence of cancer in the rectum and rectosigmoid, the necessity of a radiologic examination may be questioned. The result of such radiologic examinations performed during the years 1940—46 at the Surgical Clinic, Lund, do not argue for the necessity of such an examination. Hemorrhoidal symptoms especially bleeding, *without* objective palpation and anoscopic findings of hemorrhoids is however an urgent indication not only of the necessity of sigmoidoscopy but also of a radiologic examination of the colon.

### Summary.

In the present investigation an endeavour has been made to elucidate the frequency and relation of hemorrhoids to cancer of the colon and of the rectum. An anoscopic examination of 51 cases of cancer coli and recti revealed the presence of hemorrhoids in 19 (37 p. c.) of these cases. In a control material examined under similar conditions hemorrhoids were demonstrable in 43 cases of 104 (41 p. c.). If the cancer cases are grouped according to their location it will be found that the relative frequency of hemorrhoids is not greater in cases of low-situated cancer than in patients with tumours situated further up the colon. No support



has been produced for the establishment of a correlation between cancer and hemorrhoids.

A routine radiological examination of the colon in cases of hemorrhoids in patients over 40 years of age has been the rule at the Surgical Clinic, Lund. During the years 1940—46 no case of cancer coli was detected by this routine method and it is questioned whether this examination might not be refrained from in cases of objectively established hemorrhoids without tumour symptoms, and be reserved for such cases as have hemorrhoidal symptoms, and in which hemorrhoids can *not* be detected by anoscopy.

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From the Orthopaedic Clinic, Oslo.  
(Chief Surgeon: Docent E. Platou, M. D.)

## Arthroplasty of the Knee Joint.<sup>1</sup>

By

EIVIND PLATOU.

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As arthroplasty of the knee joint seems not to be a particularly common operation here in Scandinavia, I have thought that an account of my experiences after 16 such operations might be of interest.

A stiff knee is a very troublesome defect in young persons, even if the position is good. In case of flexed position, or, still worse, varus or valgus position of the knee, the disablement may be considerable.

My material consists of 10 men and 6 women with an average age of 28 years, the outer limits being 19 and 41 years. The cause of the stiff knee has been:

Pyarthrosis after cut in the knee in 6 cases.

»        »    operation in 2 cases.

»        »    scarlatina in 1 case.

»        »    complicated fracture in 1 case.

»        »    osteomyelitis in 2 cases.

Gonorrheal arthritis in 2 cases.

Arthritis deformans in 2 cases.

The operated knee joint has been ankylotic during 5 years and 9 months on the average, the outer limits being 13 and 2 years.

I have mainly employed the technique described by W. and A. MACAUSLAND, Boston.

Longitudinal incision on the front of the knee. The skin is loosened to the middle of each side of the knee and a V-shaped incision is then made through all soft parts, as shown in Fig. 1. The

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<sup>1</sup> Read at meeting of Scandinavian Surgical Association in Stockholm in 1947.

whole flap together with the patella is turned down and the femur is separated from the tibia. Two femoral condyles are then moulded and two corresponding sockets on the tibia, with an "eminentia intercondyloidea" 1 cm high and 1 cm wide. Altogether about  $1\frac{1}{2}$  cm of the length of the leg is removed. The

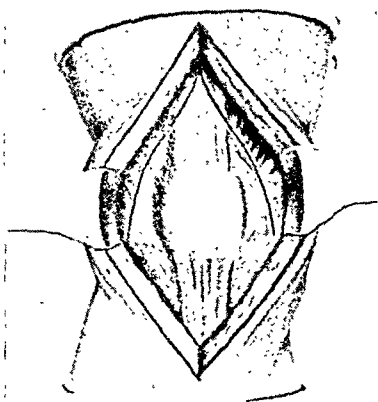


Fig. 1.

operation is performed in bloodless state and the tourniquet is then removed.

From the other thigh we then take a strip of fascia lata, about 25 cm long and 10 or 12 cm wide, with which we cover the newly fashioned ends of the joints, so as to get a double layer of fascia between them. One end of the strip of fascia is sewn fast to the anterior edge of the tibia. It is then led over the articular surfaces and sewn fast in the soft parts at the back between the femur and tibia, whereupon it is brought up over the femoral condyles. It shall be long enough to come up under the patella. The V-shaped flap of m. rectus is sewn into place, care being taken to flex the knee only  $30^\circ$ , without causing any great strain on the sutures. Owing to the V-shaped incision this can easily be accomplished. Fig. 2.

In  $30^\circ$  flexion a plaster bandage is laid from the toes up to the upper part of the thigh, during gentle traction. An opening is at once cut over the whole field of operation, so the knee can be inspected daily and a possibly occurring haematoma may be punctured. After 14 days the front part of the plaster bandage is



42



42



Fig. 3.



70/5-47.

70/5-47.



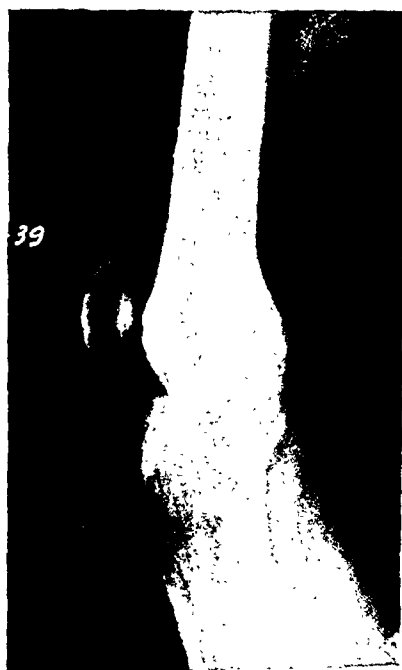
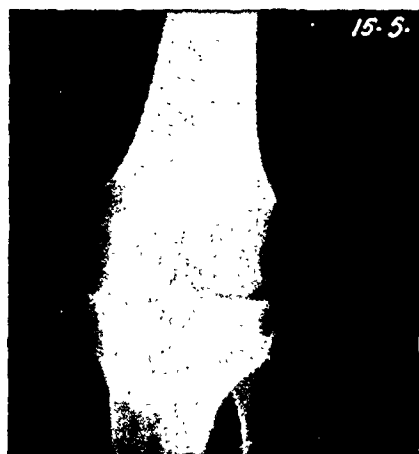


Fig. 5.

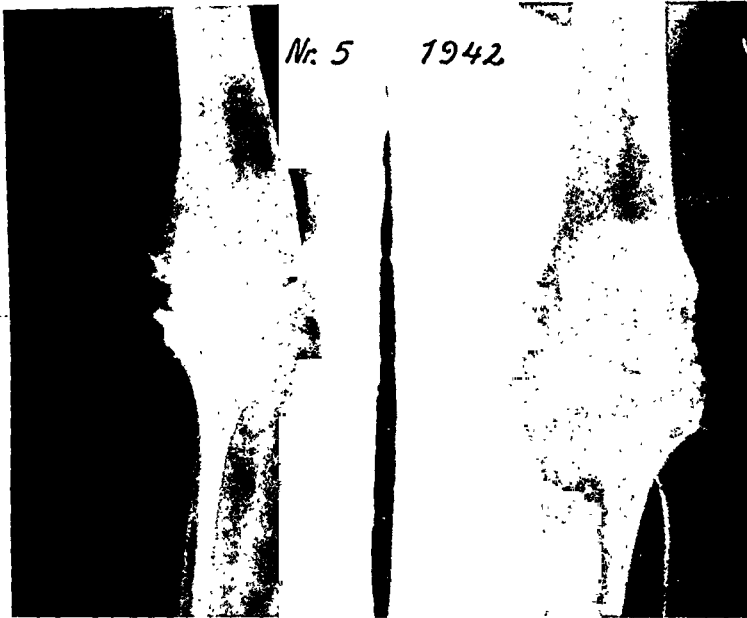


Fig. 6.

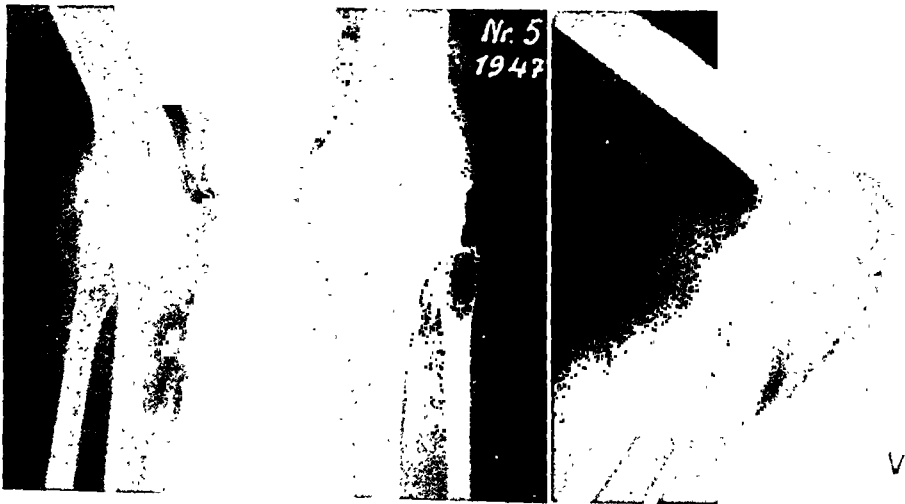


Fig. 7.

PLATOU: Arthroplasty of the Knee Joint.



Fig. 8.

removed, and passive movements are cautiously begun. After 3 weeks the patient begins to move the knee actively, with daily massage and passive mobilisation in a knee-joint mobilisator, worked by the patient himself. — After 6 weeks the patient is allowed to get up and walk with crutches. It is often very difficult

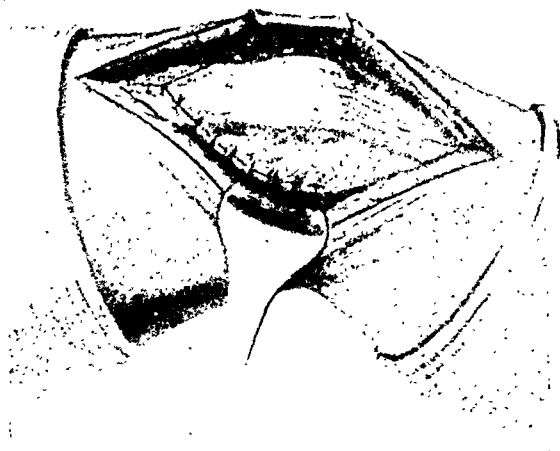


Fig. 2.

to get the mobility well up, so that in most cases I have mobilized the joint one or more times in narcosis — chiefly evipan. Occasionally is found difficult to get the knee stretched, and I have then after the third week removed the plaster bandage and applied zinc-gum traction — about 2 kg — for some weeks.

Roller skates fastened to the heels and working on an underlying wooden surface facilitate the active movement of the knee joint in the bed.

In three cases I have, from six months to one year before the plastic operation, removed puckered scars around the joint, in order to avoid the risk of secondary necrosis in such scars after the loosening of large areas of skin on the front side of the knee.

Since Penicillin came into use I have pre-treated the patients during 24 hours with 8 times 20,000 units. After the operation I injected 100,000 units into the joint and continued the penicillin treatment for 3 to 6 days.

If the lateral mobility after 8 or 10 weeks was more than  $15^{\circ}$ , which has happened a couple of times, I have employed a simple splint with articulation which prevents lateral mobility. It can be discarded after 6 months or a year.



The average time spent in the clinic was 126 days.  
 In order that an arthroplastic operation on the knee may be regarded as successful I demand three things: The knee must be free from pain, it must be stable and the patient must be able to stand on the operated leg alone and flex it about 40° — and then stretch himself up again.  
 My results are shown on the following table.

Table.

No.	Sex and age	Years after oper.	Flexion	Can put weight on flexed knee	No.	Sex and age	Years after oper.	Flexion	Can put weight on flexed knee
1	M 34	1½	10°	Yes	9	M 32	5	80°	Yes
2	M 30	2	90°	Yes	10	M 21	3½	60°	Yes
3	F 40	Ankylosis			11	M 34	Ankylosis		
4	M 19	8	90°	Yes	12	F 38	3½	90°	Yes
5	F 37	8	90°	Yes	13	F 41	3	45°	No
6	M 23	6½	90°	Yes	14	M 22	2½	90°	Yes
7	M 19	Ankylosis			15	F 25	Ankylosis		
8	F 21	6½	90°	Yes	16	M 23	¾	80°	Not yet

As is seen, the operation failed entirely in 4 cases. Patient No. 3 was operated for bilateral ankylosis of the knees after polyarthrititis. She was discharged with ability to flex the knee 40° and with good anatomical conditions. Four months later she was admitted to the clinic on account of supracondylar fracture of the femur, due to forcible flexion of the joint by her over-energetic physiotherapist. I at once applied Lane plates and after 9 weeks there was attained consolidation and mobility of about 20°, but the patient ceased to exercise the joint and in the course of a year it became stiff.

In Case 7 there came an insidious infection, probably necrosis of the fascia. When this had practically quite subsided every movement was so painful that a plaster bandage was applied after  $2\frac{1}{2}$  months, and the knee became stiff on flexion of about  $10^\circ$ .

Patient No. 11 opposed any active or passive movement of the knee. Good anatomical conditions. Uncomplicated wound-healing. The knee was mobilized three times in evipan narcosis and could without difficulty be flexed about  $60^\circ$ . After over two months' stay in the clinic he refused to allow any treatment, owing to "intolerable pain". No objective foundation for this could be found, but he shrieked aloud even on the slightest palpation in the region of the joint. When discharged, he had a capsule of the knee joint, and half a year later there came a fibrous, somewhat painful ankylosis.

In Case 15 there came a severe infection in direct succession to the operation. She had 9 years before had osteomyelitis in the lower part of the femur, with secondary pyarthrosis and subsequent bony ankylosis. I regard it as extremely probable that we had here a recrudescence of the old infection. At that time I had not penicillin. On re-examination two years later there was found bony ankylosis on slight flexion. Besides there was a fistula on the outer side of the knee. No pain. She can walk well.

In case of my first patient (No. 1), who was operated 13 years ago for ankylosis after gonorrheal gonitis, the result seems not to have been particularly good. Half a year after the operation there was only  $10^\circ$  flexion, active and passive, in spite of good anatomical conditions. I have not subsequently been able to trace him. I suppose I should have removed more of the thick rigid joint capsule.

In consequence of this experience I was rather eager to see the result of the operation when next I met with gonorrheal arthritis. The patient (No. 12) had had gonorrhea 10 years before. Here, as is seen from the diagram, the result was quite good. She has, however, a little pain in the knee.

My second patient was a 30-year-old mate, who had been operated in Japan for fracture of the patella. Pyarthrosis and stiff knee. Arthroplasty of the knee 12 years ago. Two years later he was in full work as mate. Could go up and down the ladder without difficulty. Flexed the knee  $90^\circ$  and was quite steady on his legs. One year later he died of pulmonary tuberculosis.

The necessity of being able safely to put weight on the flexed

knee I found clearly illustrated in Case 6. A year and a half after a successful plastic operation we read in the case record:

"He walks quite naturally, has no pain, flexes actively  $90^{\circ}$ , stretches fully, but cannot properly put weight on the knee at over  $10^{\circ}$  flexion. He is not satisfied."

6½ years after the operation:

"Can now safely put weight on the knee at about  $50^{\circ}$  flexion. One can just barely see that he limps a little on the operated leg. Is now very well satisfied."

Patient No. 13, who got ankylosis after infection in a complicated intra-articular fracture 12 years earlier, had a scar almost the size of a child's hand on the outer side of the knee. Necrosis occurred in this part, which, however, did not infect the joint, but it rendered the after-treatment very difficult, and the result of the operation was not quite satisfactory. There came a usually great absorption of the joint surfaces, with anterior subluxation of the crus. — The knee is unsteady, the patient has some pain and cannot put weight on the flexed knee.

Of 16 operations on the knee 4 were unsuccessful and 2 only partly successful, while 10 patients have got a knee that is free from pain and can be actively flexed to from  $60^{\circ}$  to  $90^{\circ}$ , and 10 of them can put weight on the flexed knee.

In conjunction with the paper read a demonstration was given of Case 9: A man aged 32, who two years before the operation had wounded himself with an axe in the left knee. He got pyarthrosis and ankylosis at  $35^{\circ}$  flexion. There is now, 5 years after the operation, little to be remarked about his gait. He does heavy work in a warehouse. The knee is steady, free from pain, and he can put weight on the flexed knee.  $80^{\circ}$  flexion,  $5^{\circ}$  short of full extension.

Fig. 3—4 shows radiograms from the demonstrated case, namely:

The knee before the operation.

» » over 4 months later.

» » to-day, 5 years after the operation.

If our arthroplastic operations on the knee were generally found to give such results, we would have reason to be well satisfied, but, as I shall further demonstrate, these pictures must be regarded as exceptional. It is highly surprising to see the discrepancy between the radiographic findings and the functioning of the joint.

Fig. 5. Here we have a woman aged 37 (Case 5), who five years earlier got a stiff knee after acute rheumatism. The radiogram was taken on the operation table on 11/6 1939. As is seen, my eye must have failed me somewhat, as the medial condyle has come to be rather too large.

Next we see her knee as it was over 3 years later, in 1942. The atrophy has now stopped and the joint has remained practically unchanged during these years.

Fig. 6—7 shows how the knee looked 8 years after the operation. She is very well satisfied with result. She superintends an apartment house and has for several years been going up and down six flights of stairs many times daily. Flexion, as shown in the picture, to 90°, full extension, can put weight on flexed knee.

Fig. 8. Where there was complete bony ankylosis, as in this case (No. 16). I have in the last 5 cases operated, which are not included in the present material, tried to preserve the covering surface of the tibia, in order to render it more resistant to pressure atrophy. As to whether this meant any improvement in the technique I cannot as yet express an opinion.

The material submitted is too small to admit of drawing any general conclusions. The danger of a recurrence of the previous infection does not seem to be great. In the present material the proportion of recurrence was 1 to 13.

My results are in so far satisfactory that I am inclined to think that arthroplasty of the knee ought to be performed more frequently than has hitherto been the case.

### Summary.

An account is given for 16 patients, most of whom with bony lysis after pyarthros, which has been operated, and with an observation period of up to 12 years. The operation failed 4 times. The ankylosis appeared again. In 2 cases the result was inferior. 10 patients have got a painless knee-joint, with an active flexion of 90°, and can put weight upon it with the knee bent 30—50° and can draw themselves straight again without support from the other leg.

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### **Books Received.**

- V. J. KINSELLA: "Elective Alimentary Rest" and The Elimination of So-Called "Paralytic Ileus" after Abdominal Operations. Australsian Medical Publishing Company Limited. Sydney 1948.
- V. J. KINSELLA: The Mechanism of Abdominal Pain. Australsian Medical Publishing Company Limited. Sydney 1948.
-

From the Surgical Clinic, Akademiska Sjukhuset, Uppsala.  
(Head: Professor OLLE HULTÉN.)

## **"Palliative Gastrectomy" in Cases of Duodenal Ulcer.**

By

IVAR SPAK.

"Palliative gastrectomy" signifies an operation for a duodenal ulcer, where the ulcer is left *in situ*, but the procedure is otherwise similar as in operations according to Billroth II. Palliative gastrectomies have been performed also in cases of high-lying gastric ulcers, "*pylorus-entferne*" (MADLENER), but fall outside the scope of this investigation.

The figures given by different authors for the percentage of inoperable ulcers show marked variations, ranging from 5 % (ALLEN) to 54.8 % (DELORE). In our own material palliative resections have been found to be indicated in 41 % of the cases.

Other authors, undeterred by the technical difficulties and the operative mortality, consider that all ulcers are operable (BROOKS, DENIS, MÁTYÁS, NISSEN, STEINBERG).

Palliative resection on modern lines was suggested by FINSTERER in 1918, "Resektion zur Ausschaltung". FLÖRCKEN (1923) introduced the term "palliative resection". He states that the palliative operation can be performed in one of the four following ways:

1) Prepyloric incision, 2) incision between the pylorus and the ulcer, 3) section on a level with the ulcer, 4) incision at the pylorus.

According to FINSTERER, the ideal procedure is the prepyloric incision; the postpyloric method, he states, is attended by a higher mortality (16.6 %, as compared with 5.1 % with the pylorus left in place), and should not be adopted. An incision through the pylorus is rarely attempted in view of the difficulty of closing the stump.

Palliative resection has been, and still is, a highly controversial question in the surgical treatment of duodenal ulcers, largely owing to the divergence of opinion regarding the genesis of such ulcers. The pylorus itself used to be considered as an important genetic factor (BÖRGER, CIMINATA, DOBERER, FINNEY, FRIEDEMANN, VON HABERER, HINTON, NISSEN, ORATOR, SMIDT). Later investigations, however, have made it increasingly clear that acid, and especially an excess of unneutralized acid, is the principal factor in the genesis of such ulcers (BRATTSTRÖM, BURK, CLAIRMONT, FINSTERER, GULEKE, IHRE, KRABBEL, LANNIN, LERICHE, MÖRL, SOSTEGNI, STRÖMBECK, WANGENSTEEN, ZAHUMENSZKY).

In the production of acid, which is stimulated in different ways, we can distinguish three phases: 1) Secretion due to mental excitation; this secretion remains unaffected even after resection. 2) The chemical phase, which in a normal stomach is probably due to the irritation caused by food on the non-acid-secreting glands in the pylorus and antrum region by a hormone, termed gastrin (EDKINS), which affects the acid-producing fundus cells. This effect is greatly modified, or completely disappears after resection of the antrum part (ENDERLEN and ZUKSCHWERDT, SMIDT, UVNÄS, ZUKSCHWERDT and BECKER). 3) The intestinal phase, which, however, does not play any important part in the genesis of duodenal ulcers, nor is appreciably modified after resection, and therefore is of no interest in this connection.

We also regard an excess production of unneutralized acid as the principal factor in the genesis of ulcers. Once the acid-exciting mucosa has been removed, we see no risk in retaining the pyloric muscle. No importance can be attached to this muscle in regard to the production of acid either theoretically or in practice (ZUKSCHWERDT and BECKER).

### Indications.

The indications for palliative resection are particularly clear in the case of ulcers penetrating to the pancreas, where injury to the pancreas or gall ducts might be entailed by radical operation. The risk of damaging the large excretory ducts of the gallbladder and pancreas is very great, especially in view of the possibility that their position may be changed by involvement in the large contracting scar tissue formed by penetrating ulcers.

Thorough studies of the anatomy of the pancreatic ducts have been made by CLAIRMONT and PLENK. The principal excretory duct is the *ductus Wirsungianus*, which, however, is rarely damaged, owing to its position. The accessory duct of the pancreas, *ductus Santorini*, on the other hand, shows a closer connection with the ulcer. HULTÉN has also drawn attention to the great risk of injuring the large excretory duct of the pancreas, in view of the little known fact that it curves upwards behind the duo-

denal bulb and does not — as stated in anatomical textbooks — run straight to the duodenum. See the attached illustration.



Cholangiogram: The pars horizontalis sup. and the duodenal bulb are filled, in addition to the pars descendens duodeni, and we see that the arch of the pancreatic duct is crossed by the duodenal bulb.

In many cases the common bile-duct is also involved in the scar tissue of the ulcer, especially when it reaches far down into the descending part of the duodenum and is thus brought close to the duodenal papilla, or when a large ulcer in the horizontal part of the duodenum involves the hepatoduodenal ligament. The common duct is thus liable to arrosion on the anterior side, a "choledochoduodenostomia interna" (FINSTERER), and will then be exposed on resection with the usual technique (DEMEL, MILLER).

As KIRSCHNER and PHILIPPIDES point out, heroic operations may succeed. An embedded choledochus duct may be dissected out; the duodenal papilla may be transplanted (BRÜNING, JOST, KRABEL, LAHEY, PHILIPOWICZ); the hepatic artery can be detached or even sutured; the major part of the pancreatic head can be resected, and, even in cases where the material is unsatisfactory, the duodenal stump may be tolerably closed. Such operations, however, are attended by serious risks.

Injuries to the portal vein and hepatic artery need rarely be taken into consideration, though apparently they sometimes occur. One of our cases is instructive in this respect:

*Man, aged 52.* Treated for a duodenal ulcer in 1914. Afterwards in good health for 16 years. Perpetual new symptoms from 1931 onwards. An operation in 1936 revealed the following: There was an extensively radiating scar on the anterior side of the duodenal bulb and an edema about 1 cm in thickness in the hepatoduodenal ligament. Obliquely across the ligament, and quite close to the minor side of the bulb, ran a pulsating artery (4 mm in diameter), branching off from the right gastric artery to the liver and doubtless serving as its main branch. The rear side of the bulb adhered closely to the pancreas.



A radical operation would have involved risk to the hepatic artery, with disastrous results for the blood supply of the liver.

In cutting out a penetrating ulcer, there is a great risk of damaging the pancreas, with the consequent development of a pancreatitis (KÜTTNER, BSTEH) and a risk of loosening the sutures of the duodenal stump. Many cases of injury to the pancreas with a fatal issue have been published (CEDERMARK, CLAIRMONT, DOBERER, EURÉN, FINSTERER, KÜTTNER).

There are indeed several ingenious methods for the closure of the duodenal stump (BROOKS and MEACHAM, BSTEH, BURK, DENIS, DENK, DOBERER, GULEKE, VON HABERER, HOLUBEC, INSUA, JACBOVICI, MÁTYÁS, NISSEN, STEINBERG) but the risk is nevertheless very considerable. FROMME estimates the occurrence of duodenal fistulas at 5 percent and the mortality from that cause at 50 percent.

*The principal advantage of palliative resection is the greater safety in the closure of the duodenal stump.*

### Complications.

The main risks in palliative resection are bleeding from the remaining ulcer and perforation. Several cases of postoperative bleeding have been published (FINSTERER, FLÖRCKEN, FROMME, HINTON, HOLLENBACH, MÖRL, ZUKSCHWERDT). The last-mentioned author, on the other hand, has published some cases in which the bleeding stopped after the operation.

Among our cases there was a woman, aged 60, who immediately before operation had had a severe hemorrhage and a grave anemia with a hemoglobin figure of 35 percent, which was not improved by repeated blood transfusions. Despite the patient's bad general condition, the operation was performed as a typical palliative resection, as there seemed to be no other alternative. *Recovery was completely free from complications.* The patient has remained completely free from symptoms during the three years she has been under observation.

The risks of postoperative hemorrhage are greatest during the days immediately succeeding the operation; thereafter the ulcer heals rapidly (FINSTERER, GÜTIG, KNERINGER, RIENHOFF).

A postoperative hemorrhage, however, need not always be attributed to the method: as with bleeding after a radical operation, its cause may doubtless be looked for elsewhere in several of the published cases. A hemorrhage may emanate from the

suture line, from erosive gastritis etc., as after a radical operation according to Billroth II (BRATTSTRÖM).

Perforation of an ulcer that has been left in situ is particularly liable to occur when another, anteriorly situated, ulcer is present at the same time; the latter, however, can be inspected at operation and, if necessary, be covered with omentum. An important point is to avoid traumatization of the area menaced by perforation. If the duodenum is stretched on order to enforce a mobilization for a doubtful closure, the risks will be considerably increased.

### Peptic Ulcer of the Jejunum.

It has been indicated above that the pyloric musculature may be left intact, as it cannot be considered to be a factor of any importance in the genesis of a primary ulcer nor of a peptic ulcer of the jejunum. Several cases of peptic jejunal ulcer after palliative resection have indeed been reported. In many of them, however, either it is not stated in the operation report that the mucosa in the antrum was removed, or it is evident that the excision was incomplete. ZUKSCHWERDT and HORSTMANN (1936) in a statistical survey of 1,415 palliative resections, recorded the occurrence of peptic jejunal ulcer in 1.8 percent or the *same percentage as for radical operations*.

A significant report on this subject has been published by ALLEN. Among 9 cases of palliative operation in which he had left the antrum mucosa intact he noted peptic jejunal ulcers in five but no peptic ulcer was observed after excision of the mucosa in 20 other cases. Among the 98 cases of duodenal ulcer treated at this hospital with palliative resection (see Table 3 below) not a single peptic ulcer developed.

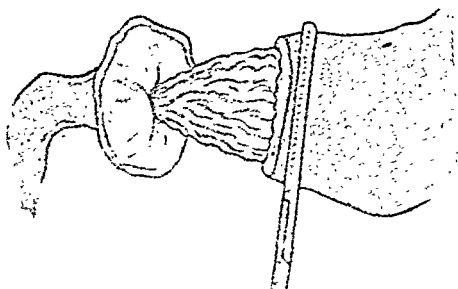
### Technic.

In FINSTERER's above-mentioned method, the stomach is divided at the antrum a few centimeters proximally to the pylorus. In certain cases the incision may be made postpylorically; this, however, considerably complicates the operation and entails a higher mortality owing to the greater difficulty in closing the duodenal stump.

Our material includes merely some ten postpyloric operations, one of which led to death. In the fatal case a palliative operation had been resolved upon too late, when the dissolution had al-

ready proceeded too far. *It can scarcely be too strongly emphasized that the palliative operation must be systematically planned, not resorted to as an emergency.*

Several different methods have been proposed for the treatment of the antrum stump. We usually ligate the blood vessels down to 4—5 cm from the pylorus; a clip is then placed over the stomach, and the serosa and the musculature is treated with diathermy. The mucosa is not cut: we insert the diathermic needle into the loose submucous layer down to the pylorus, the musculature being stripped off like a cuff. See the attached illustration.



The detachment is easily effected, though in the immediate vicinity of the pylorus the mucosa is more closely connected with the muscular wall. The mucosa here assumes a different appearance: it gets thinner and finally ruptures. This, in conjunction with a usually distinctly marked torus pylori, is a sign indicating that the resection of the mucosa has proceeded far enough.

We do not make any suture of the mucosa, but leave the mucosa canal open. When the flow of blood has been carefully stanching, the muscularis "funnel" is invaginated, so as to form a solid, walnut-sized collar in the pylorus. A sufficiently large muscularis "funnel" must be allowed for, as the invaginated portion will meet with resistance at the pyloric ring and cannot be driven past it; a width of 4—5 cm is necessary, especially if the musculature is hypertrophic. The bleeding that ensues when the mucosa is dissected out seldom causes trouble. Should no bleeding ensue, this is an indication that the ligation of the blood vessels has been driven too far, with consequent risk of necrosis of the stump.

Some operators, including FINSTERER, KOVÁŘ, FROMME, HELLSTRÖM and PLENK either close the mucosa after its detachment with a suture or ligate it. Instead of invaginating the muscularis "funnel", some operators sew the front and rear sides to one another (FINSTERER, FROMME, PALLIN, PLENK) with a mattress suture. Some do not resort

to diathermy, but detach the mucosa either bluntly or sharply (FROMME, PLENK).

When the canalis stump has been invaginated, we proceed as in the Billroth II method and arrange a gastroenterostomy along the whole cross section of the stomach. As a rule it is arranged retrocolically, but if the mesocolon is very fat, it is placed in front of the transverse colon. HULTÉN always makes an entero-anastomosis between the afferent and efferent loops, in order to obviate retrograde filling and stagnation in the duodenum. A detail of extreme importance in preparing the serosa-muscularis "funnel" is to keep its vascular supply intact by taking care not to detach the gastrocolic ligament and the lesser omentum below the level of the resection line, so as to avoid causing anemia, necrosis, and leakage from the stump (FINSTERER, FROMME, GRETTE, KLEINSCHMIDT, PERMAN). If the blood vessels are ligated too far, it can be distinctly seen at operation that the stump is becoming anemic.

In case the operator objects in principle to palliative resection, FINSTERER recommends a modification, the two-stage procedure. At the first stage the antrum part is closed by a simple operation and four to six weeks later the pylorus itself and the whole ulcerated area is extirpated, which can be done without difficulty after the subsidence of the acute lesion. The same procedure is adopted by MELTZER and MC KITTRIC.

## Results.

To judge by the statistics for recent years, tabulated below, the results of correctly performed palliative resections have been satisfactory:

Table 1.

	Year	Mortality	Followed-up	Good results	Peptic jejunal ulcer
ZUKSCHWERDT and HORSTMANN .....	1936	5.7 %	1,415	92.5 %	1.8 %
FLÖRCKEN .....	1939	3.7 %	213	96.2 %	0.88 %
FINSTERER <sup>1</sup> .....	1940				
	Py left	5.1 %	90	88.8 %	5.5 %
	Py resected	16.6 %	35	88.5 %	0 %
THORGENSEN .....	1941	6.7 %	98	93 %	0 %
BRUSGAARD .....	1946	0 %	27	89.2 %	0 %

<sup>1</sup> FINSTERER's statistics are obscured by the fact that during an earlier period he did not excise the mucosa in the antrum part, with the consequent development of peptic jejunal ulcer. During the last ten years he has had no case of peptic jejunal ulcer.

In Sweden the following statistics on the subject have been published:

Table 2.

	Year	Number	Mortality	Followed-up	Good results	Peptic jejunal ulcer
PALLIN . . . . .	1932	30	6.7 %	16	94 %	1
FRIBERG . . . . .	1936	68	4.4 %	65	87.7 %	0
LANDELIUS . . . . .	1937	25	24 %	—	—	—
CEDERMARK . . . . .	1942	22	0 %	—	—	—
JOSSON . . . . .	1945	123	5.7 %	100	94 %	0
Uppsala cases	1948	98	2 %	83	92 %	0

### Follow-up Examination.

Our follow-up examination comprises all the cases of duodenal ulcer treated at the clinic with palliative resection during the period 1936—1945. All the radical resections (*i. e.* in which the ulcer was excised at operation) performed in the course of the same period served for the purpose of control. An objective estimate of the results is difficult, but *the value of the follow-up examination lies in facilitating a comparison with groups* thus examined under similar conditions. The resections were performed by several different operators, but with an approximately equal percentage distribution in both groups. The indications were uniform, whence the groups are quite comparable. Nearly all the patients presented themselves for personal examination; 14 who were unable to attend the examination filled in detailed questionnaires, 5 had died of intercurrent diseases and one (an American national) was inaccessible.

The distribution of the operations for duodenal ulcer from 1936 onwards is shown in the subjoined Table 3.

The mortality for palliative resections is thus 2 percent, whereas for Billroth II it is 5.5 percent. For both groups together the mortality figure is 4.2 percent. Billroth I for the treatment of duodenal ulcer is now falling into disuse at this hospital. Gastro-enterostomy is adopted only in exceptional cases, chiefly elderly patients with stenosis.

The follow-up examination did not include patients with shorter periods of observation than one year. The number and sex of the patients thus examined, apart from those who had died from intercurrent diseases, is shown below in Table 4.

Table 3.

Year of op.	Billroth I	Billroth II	Palliative resection	Gastro-enterostomy
1936.....	17 (1 death)	8 (1 death)	6	6
1937.....	12	8	3	2 (1 death)
1938.....	17 (1 death)	14 (1 death)	4	3
1939.....	14 (1 death)	3	10	6
1940.....	6	9 (1 death)	12 (1 death)	1
1941.....	6	9 (4 deaths)	21	1
1942.....	13	14	9	4 (1 death)
1943.....	17	16 (1 death)	12 (1 death)	1
1944.....	5	26	10	2
1945.....	4	35	11	2
Total	111 (3 deaths) 3 %	142 (8 deaths) 5.5 %	98 (2 deaths) 2 %	28 (2 deaths) 7 %

Table 4.

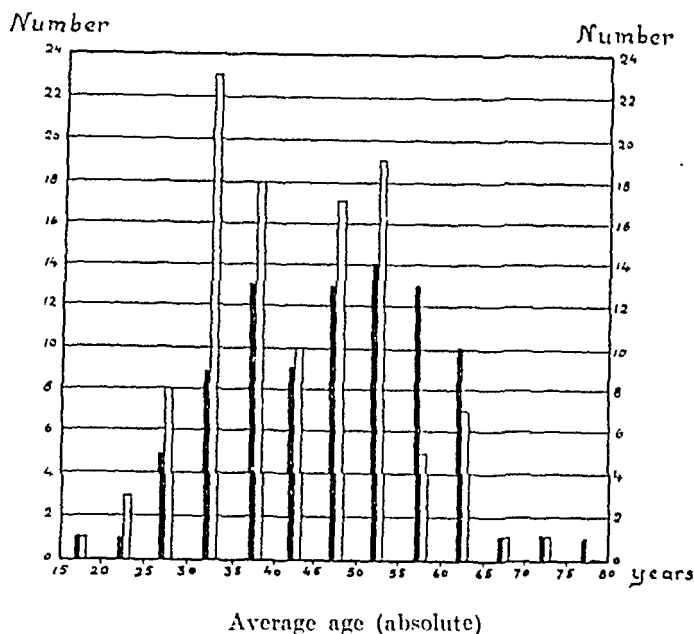
	Palliative resection	Billroth II
Number .....	83	102
Sex .....	67 men, 16 women	77 men, 25 women
Ratio .....	4.2 : 1	3.1 : 1

The palliative group includes 10 cases of postpyloric resection. The age at the time of operation is shown in the following Table 5.

The patients subjected to palliative resection (both men and women) were thus on an average about five years older at the time of operation, which corresponds well with the fact that the palliative operation was resorted to in cases where the disease had been more severe and had reached a more advanced stage. The proportion of men to women as well as the age distribution in the two groups being approximately the same, no distinction between the sexes will be made in the following.

Complications in connection with the operations occurred in a small number of cases, as shown in the following Table 6.

The first group comprises complications from the duodenal stump, consisting of suspected or verified abscesses, in all cases presumably due to stump insufficiency. These complications include two very significant cases in which palliative resection was resolved upon too late. In the first case it was not until the detachment of the duodenum had met with insuperable obstacles that the stump was closed with considerable difficulty below the pylorus. The patient was discharged after ten days, but returned

TABLE 5

	Palliative resection		Billroth II	
	Men	Women	Men	Women
Age in years .....	46	50	41	45
Average .....	47 years		42 years	

Table 6.  
Complications.

	From the duodenal stump		Other complications	
	Palliative resection	Billroth II	Palliative resection	Billroth II
< 45 years .....	5.5 % (2)	7 % (4)	5.5 % (2)	15.5 % (9)
> 45 years .....	6.5 % (3)	2 % (1)	6.5 % (3)	18 % (8)
Total	6 %	5 %	6 %	16.5 %

three weeks later with a subhepatic abscess, which, however, healed conservatively. In the second case, the stomachal blood vessels were ligated down to the pylorus, at first with the intention of performing a radical operation. The stump was inadequately supplied with blood with consequent postoperative insufficiency. It healed, however, after drainage. In another case

the duodenal mucosa was treated with diathermy through the pylorus ("Mukoklase" according to the method of JACOBOWICZ). The duodenal stump was presumably injured by this procedure.

The two cases of mortality in the palliative resection group (see Table 3) are not included in Table 6; both are significant.

*Case 1.* (Record No. 1477/1940). Man aged 46, who had suffered for 8 years from severe ulcers. Palliative resection. In view of a tendency to thrombosis, heparin treatment was given after the operation. Four days later this treatment was abandoned, owing to a probable abscess of the stump that was incised after five days. Later large haemorrhages through the wound. Death 1 month after operation. The postmortem showed that the distal stump was quite open and surrounded by a large infected haematoma.

Probably due to the heparin treatment, a haematoma developed around the stump; it was infected and the sutures loosened.

*Case 2.* (Record 3915/1943). Man aged 36, with a 12-year history of ulcer. A palliative operation was performed as in the first case, with the difference that the operator first tried to free the ulcer, not resorting to palliative resection until the detachment from the pancreas had failed. All the blood vessels to the pyloric region had then been ligated, so that the circulation was defective; the stump opened, and the patient died on the 13th day of peritonitis. The postmortem revealed an abscess the size of a thumb-end behind the duodenal stump, necrotic pancreatitis and diffuse peritonitis.

The five cases of complications from the stump in the Billroth II group (Table 6) all showed pancreatic irritation. In one case, after a considerable lesion of the pancreas, drainage was arranged and at first resulted in a copious outflow of pancreatic juice. None of the four other cases were drained; nor was incision required.

The cases of death from Billroth II are briefly described below:

1. (Record 3033/1943). Man, aged 59. Large ulcer crater, penetrating into the pancreas. The bottom of the ulcer was cauterized. Postoperative peritonitis, proceeding from the bottom of the ulcer.

2. (Record 1242/1941). Man, aged 61. There was an ulcer adherent to the pancreas below the pylorus. Postoperative peritonitis, proceeding from a local abscess of the stump evidently owing to the defectiveness of the wall at the place of penetration. A suture insufficiency had occurred with resulting peritonitis.

3. (Record 760/1941). Man, aged 61. The operation showed a callous hardening 2—3 cm below the pylorus. The postmortem revealed a diffuse peritonitis, presumably due to pancreatic damage.

4. (Record 910/1938). Man, aged 34. This case was reported in detail by HULTÉN in 1939. — In detaching the ulcer adherent to the pancreas,



the duct of Wirsung was damaged and drainage was therefore arranged. The immediate death cause, however, was an embolism in the lung.

5. (Record 1470/1941). Man, aged 27. An ulcer penetrating towards the pancreas was detached and the bottom of the ulcer was burnt out with diathermy. On the 10th day an abscess cavity around the stump was incised. Afterwards a copious efflux of bile, proceeding from the wound. 2 weeks later cholecystojejunostomy was performed with good effect; the pancreatic juice, however, continued to flow from the fistula. The postmortem showed that the common bile duct as well as the duct of Wirsung had been damaged. This damage was most probably caused by the diathermic treatment of the ulcer floor.

In all these cases the conditions found at operation should have indicated a palliative treatment, which would indubitably have led to a more fortunate issue. — The three other deaths in the Billroth II group are not attributable to the method of operation, and the causes may therefore be passed by. — The group "other complications" in Table 6 includes sequelae not connected with the stump, such as abscesses of the abdominal wall, pneumonia, thromboses with or without emboli, and two cases with mechanical obstructions to evacuation.

The investigation thus shows that complications from the distal resection stump, which is the principal risk, did not occur to any extent among the patients subjected to palliative resection. *The deaths clearly argue in favour of that treatment.*

### Postoperative Hospitalization.

No difference could be found between the groups regarding cases without complications (13 days). For cases with complications from the distal stump, five cases in each of the groups, the average hospital stay was 42 days for palliative resection and 19 days for Billroth II. If all complications are included, on the other hand, the hospital stay is 32 days for palliative resection and 36 days for Billroth II. The cases are few in number, and chance may have played a part.

### State of Health.

According to a classification made by HORSLEY and previously adopted in Swedish publications, patients are ranged in four groups with respect to their state of health, viz.

1) "Symptom-free", being those who have not had any stomach troubles on ordinary diet, and who had not had any symptoms of this kind for some few months after operation.

2) "Greatly improved". Practically symptom-free, but who have occasionally had slight discomfort from flatulence on ordinary diet. These symptoms do not affect the patient's regular occupation or profession and do not indicate any special treatment, except possibly a slight restriction of the diet. Patients suffering from mild anemia have also been included in this group.

3) "Slightly improved", comprising those cases where the symptoms are pronounced, although the condition is better than before the operation. The patients have considerable discomfort from flatulence or other gastric symptoms.

4) "Unimproved", comprising those cases where the patients are evidently still in bad health or worse than before the operation.

Groups 1 and 2 are usually regarded as showing "satisfactory results".

The average period of observation as a whole is approximately the same, being 4.4 for palliative resection and 4.1 years for Billroth II. As indicated by Table 7, there is no marked difference between the two methods; this applies also to the "satisfactory results".

Table 7.  
*State of Health.*

Group	Palliative resection		Billroth II	
	Number	Percentage	Number	Percentage
1...	58	$69.9 \pm 5.0$	70	$68.6 \pm 4.6$
2...	18	$21.7 \pm 4.5$	21	$20.6 \pm 4.0$
3...	5	$6.0 \pm 2.6$	8	$7.9 \pm 2.7$
4...	2	$2.4 \pm 1.7$	3	$2.9 \pm 1.7$
Total	83	100.0 %	102	100.0 %

*Thus, broadly speaking, the state of health in the patients subjected to palliative resection has been found to be neither better nor worse than in those subjected to the Billroth II operation.*

As regards group 3, there were 4 cases of anemic symptoms, 4 of dyspeptic and 5 of both anemic and dyspeptic symptoms. No difference was noted in this regard between men and women.

Among the unimproved cases subjected to palliative resection, a young man, aged 31, was suffering great postcoenal discomfort from rapid evacuation of the stomach. Four years after the resection, a change-over was made to the Billroth I operation, after which the patient improved. The second case, a female teacher, aged 39, is a typical neurotic, who daily consumes about ten different kinds of medicine. In view of this neurosis it may be questioned whether an operation should have been performed at all.

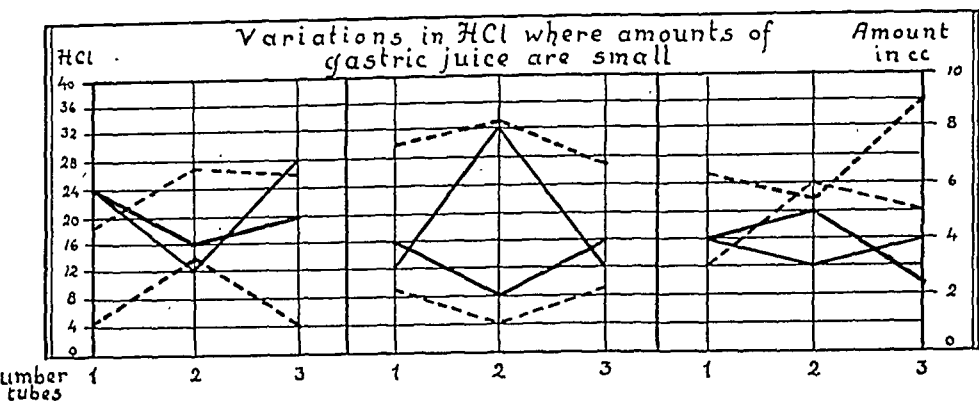
Among the unimproved patients subjected to the Billroth II operation, there was a neurotic and alcoholic, aged 43, who had been repeatedly hospitalized. He was now suffering chiefly from discomfort due to rapid evacuation and from symptoms of gastritis. There was also a woman, aged 48, with severe anemia and marked dyspeptic symptoms. This patient moreover had been suffering for twenty years from large, incurable ulcers on the legs, which impaired her strength. The third case was a married woman, aged 29, who had been reoperated owing to faulty connection of the gastroenterostomy loop. Three months after operation she was laid up with an infected tubal abortion. Recovery was complicated by a resistant peroneal paresis. During three years of observation she had been repeatedly treated for severe dyspeptic symptoms and grave anemia.

### Occurrence of Acid.

Among other details, we note firstly the occurrence of free acid. A fractionated test-breakfast was given, with the patient in a recumbent position (according to the method of STRÖMBECK) in order to reduce the rate of evacuation. This test took 1—3 hours. As a stimulant, 0.20 gram of caffeine was used. As the test was intended for comparison between two similar groups, stimulation with histamine was not considered necessary. The acid values found, however, are not to be regarded as "actual" indications of the capacity to secrete acid, but merely as "potential" (HOFFMANN).

The results of the titration are difficult to judge. The amount of gastric juice drawn off, owing to the rapid emptying of the stomach — which, however, must be presumed to be less marked than in a standing position — in many cases does not amount even to 10 cc, furthermore the determination of the acidity by the usual methods is uncertain, which may possibly be due also to defects in the graduation

Table 8.



Marking: Unbroken lines = amount of gastric juice in cc.  
 Broken > = > free HCl.  
 Curves of the same colour are connected.

of the tubes used in Sweden for these tests. As shown by Table 8, higher values were obtained in several cases in which a smaller amount of gastric juice was drawn off.

An admixture with bile and pancreatic juice was observed in several tubes. In view of their low neutralizing power (ENDERLEN, FREUDENBERG, REDWITZ and PERMAN), these juices, however, presumably had no marked effect on the acid figures. In the few cases where the admixture of bile had been considerable and free acid had not occurred, the test was renewed. In none of these cases, however, could acid be detected on the renewal of the test. For the purpose of comparison on broad lines, and in view of the unreliability of the acid figures, only the occurrence of free acid is noted in this investigation. See Table 9.

Table 9.

	Palliative resection	Billroth II
1—4 years .....	26 % (38 cases)	39 % (57 cases)
5—9 years .....	17 % (30 cases)	27 % (30 cases)
1—9 years .....	22 ± 5 %	34 ± 5 %
Difference 12 ± 7 %		

The figures for the palliative resection group are thus lower, but the difference,  $12 \pm 7$  percent, is not statistically significant. The investigation has in fact shown that *there was no significant difference in the production of acid between the compared groups.*

UFFREDUZZI estimates the anacidity at 63 percent, RIENHOFF at 40 percent. Our cases show for palliative resection 78 percent and for Billroth II 66 percent. The difference, nevertheless, is not statistically significant.

Quantitatively, the acid values were as a rule low. In only four cases (three of which were palliative resections) — where at least 10 cc of gastric juice had been obtained — values of 50 or more were found. In one of the palliative resection cases the pylorus had been extirpated, in the two others the mucosa in the remaining antrum part is reported to have been removed. The highest figure, 60, was found in connection with a Billroth II operation, in which, however, merely the lower third part of the stomach had been resected because of a previous gastroenterostomy. All these patients are completely symptom-free. In fact, as previously shown by HOFFMANN, KONJETZNY, TOMODA and WYMER, freedom from symptoms is often found even where the acid values are high. — Preoperatively, a test-breakfast is the method always adopted at this hospital for ascertaining the condition of the gastric juice. Postoperatively, it was used in only three of the cases subjected to the follow-up examination. These cases, all of which had been treated with palliative resection, are summarized in Table 10. The present figures are in fact considerably lower than preoperatively. It is noteworthy that the first-mentioned case, a woman aged 52, who postoperatively had shown an achylia refractory to histamine, now nevertheless has a moderate acid value after stimulation with caffeine alone.

Table 10.

*Palliative Resection Only.*

Sex	Age at op.	Date	HCl	Total acidity	Notes
Woman ..	52	before op.	80	93	Caffeine
		after 12 days	0	22	Histamine
		after 5 years	15	27	Caffeine
Man .....	56	before op.	108	120	Caffeine
		after 13 days	30	40	» (7 cc)
		after 6 years	40	55	» (5 cc)
Man .....	33	before op.	86	110	Caffeine
		after 40 days	50	70	»
		after 5 years	+	20	»

## Dyspeptic Symptoms.

Table 11.

*Number of Dyspeptic Symptoms.*

Explanation in the text.

	Palliative resection	Billroth II
Patients with one symptom .....	15	25
» » two symptoms .....	12	16
» » three » .....	3	7
» » many » .....	2	4
Symptom-free .....	51	48
Not observed .....	—	2
Total number .....	83	102
Percentage with symptoms .....	$39 \pm 5 \%$	$1 \pm 5 \%$
	Difference $12 \pm 7 \%$	

The term "dyspeptic symptoms" includes lassitude after meals, eructations, inability to tolerate fat food or milk and discomfort from flatulence or pain. Figures 1—4 indicate the number of these symptoms felt by the respective patients. Thus, 39 percent of the patients had more or less marked symptoms from palliative resection, and 51 percent from Billroth II. The difference,  $12 \pm 7$  percent, however, is not statistically significant.

## Increase in Weight.

Table 12.

Number of cases .....	71	87
Percentage with increase in weight .....	$71.8 \pm 5.3 \%$	$51.7 \pm 5.4 \%$
Average increase in weight, kg .....	3.7	1.9
The difference is $20.2 \pm 7.6 \%$		

The figures are reckoned on the basis of the date of admission for operation and the present date. Cases in which previous data regarding the weight were not available were not included. In the palliative resection group there is 1.8 kg higher increase in weight. The difference is "probable". The higher increase in weight in the palliative resection group is presumably connected with the fact that in this group the patients had as a rule been in a worse con-

dition before operation. The ulcer symptoms had lasted longer, causing greater emaciation, and the increase in weight was therefore more noticeable. In both groups the postoperative increase in weight was more marked during the first few years.

### Feces Findings.

WEBER's test was made in all the follow-up examinations. In some cases the tests were positive, but control tests when the patient had been put for some days on a meat-free diet did not show anything noteworthy. Microscopic examination was not made.

### Blood Values.

This investigation will be published as a separate article.

### Entero-anastomosis.

In order to avoid postoperative retrograde distention and stagnation in the duodenum with the risk of rise of pressure and perforation of the remaining ulcer, HULTÉN always establishes an entero-anastomosis between the afferent and efferent loops. The expediency of this procedure has been discussed in the literature. All operators, however, are agreed that entero-anastomosis, in conjunction with Roux' Y-shaped anastomosis, predisposes for peptic jejunal ulcer. FINSTERER also considers that entero-anastomosis in resections with an ordinary gastrojejunostomy loop involves a greater risk of peptic ulcer. FLÖRCKEN, on the other hand, always makes an entero-anastomosis and reports peptic jejunal ulcer in only 0.88 percent of the cases. In our material there is not a single case of such ulcer.

Table 13.

	Palliative resection		Billroth II	
	Without entero-anastomosis	With entero-anastomosis	Without entero-anastomosis	With entero-anastomosis
Group 1 .....	30	27	45	25
Groups 2-4 .....	17	8	19	13
Percentage symptom-free .....	63.8 %	77.1 %	70.3 %	65.8 %

The sub-groups with and without entero-anastomosis show no significant difference in the percentages of symptom-free cases. We consider therefore that we can contradict the statement that entero-anastomosis predisposes for peptic jejunal ulcer. On the other hand, the investigation does not indicate that entero-anastomosis has been of any statistically verifiable use. This, however, is difficult to show in figures, and it is conceivable that entero-anastomosis in some particular case may have helped to save life.

### Summary.

The follow-up examination reported here comprised the cases of palliative resection at the Uppsala clinic during a nine-year period, exclusive of patients who had been under observation for a shorter time than one year. The special value of the investigation lies in a comparison with the radical operations performed during the same period. 83 of the patients followed-up had been subjected to palliative resection, 102 to Billroth II. Only one patient could not be traced. The patients subjected to palliative resection were, on an average, five years older at the time of operation.

The complications are found to be in approximately the same proportion in the two groups. The importance of well-planned palliative resection — which should not be resorted to as an emergency operation — is emphasized. Two cases are reported, in which postoperative complications might have been avoided if this rule had been observed. The operative mortality, two cases of palliative resection and eight of Billroth II, is reviewed. Among the latter, the author points out five deaths which could probably have been avoided if the operator had done a palliative resection instead of a radical operation.

The postoperative hospitalization shows no difference between the two groups.

The state of health at the follow-up examination proved to be very good, with satisfactory results in 91.6 percent of the cases of palliative resection and in 89.2 percent of the cases of Billroth II. The less satisfactory and the poor results are analyzed. The causes are found to be common to the two groups.

The occurrence of acid was investigated by a fractionated test-breakfast. The acid figures for palliative resection are on the



whole lower than for Billroth II. This fact clearly shows that the pyloric part where the mucosa had been removed, but which otherwise had been left intact, had no bearing on the secretion of acid nor on the postoperative development of peptic ulcers in the jejunum.

Dyspeptic symptoms were found in approximately the same proportion in both groups, though, roughly speaking, they were less marked after palliative resection. The increase in weight, on the other hand, is more marked as regards the latter cases.

The blood status was investigated with regard to haemoglobin percentage, erythrocyte count and serum iron. In the total material there was a mild anemia of the iron-deficiency type, which confirms previous findings. Likewise in accordance with earlier observations, the women seemed to show a greater tendency to anemia than the men. No difference in this respect could be found between the two groups. The occurrence of free acid was shown to have no bearing on the frequency of anemia.

Finally, it is shown that the establishment of an entero-anastomosis does not predipose for the development of peptic ulcers of the jejunum.

This investigation shows that no essential difference can be found between the effects of the two methods of operation, either as regards complications or the state of health, even a long time after the operation. As palliative resection in many cases is technically easier and less hazardous and therefore burdened with a lower mortality, this operative procedure should be practised on a larger scale.

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## **An Attempt to Evaluate the Different Modern Methods for the Prevention and Treatment of Thrombo-embolism.**

By

J. P. STRÖMBECK.

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In the surgery of the last half century many methods have been suggested for the prevention and treatment of thrombosis and its complications. It may indeed be said that for a long time the multiplicity of these methods and their alleged infallibility did not strengthen one's confidence in them. On the other hand for a decade now we have had at our disposal a few reliable methods which seem to be effective.

Two main types of method have been tried out: (1) *early movements in bed and early ambulation*; (2) *anti-coagulant methods*. Of these two types only the first has been used to any large extent by itself, while the second has either been used by itself or been combined with some degree of movement. For the most part it is these two procedures that have evoked lively discussion during the forties, especially in the Scandinavian countries but also in Anglo-Saxon (and particularly American) publications on the subject. So much experience now seems to have been accumulated that it is about time to venture to compare the value of the different methods that have been suggested and of their modifications. It goes without saying that my comparison will be made primarily on the basis of experience obtained in the Surgical Clinic at Lund. In this south-Swedish clinic the frequency of thrombosis has for a long time now been thoroughly investigated and found to be remarkably high (about 10 per cent of postopera-

tive cases). Since 1941 tests have been carried out especially with the anti-coagulants, first heparin and then chiefly dicumarin.<sup>1</sup> During 1946 we conducted a series of tests which, I hope, will admit, as objectively as possible, of a comparative evaluation of the different preventive methods, and especially of early ambulation and of dicumarin as a prophylactic.

Let me say at the outset that we have had no practical experience of the bold and radical method now employed prophylactically and in cases of embolism at leading American clinics by HOMANS, ALLEN, LINTON, DONALDSON and others, where bilateral ligation of the femoral or iliac or even of the inferior vena cava is carried out at the operation or on the first sign of leg-thrombosis or pulmonary embolism, as the case may be. The method has from the beginning seemed to us rather destructive and unnecessary in view of the good results that can be obtained without ligations in such cases. Nor have we had any experience of Havlicek's ultra-violet-ray method with open abdomen, or of Ochsner's sympathetic novocain block.

An evaluation from the theoretical point of view of the different methods of prevention and treatment would certainly be easier to undertake if we had a more detailed knowledge of the etiology and pathogenesis of thrombosis. Virchow's triad of causal factors (now almost 100 years old) — venous stasis, altered composition of the blood, intima lesion — still for the most part represents the extent of our knowledge. Opinions are still divided concerning the relative importance of these basic factors and also concerning the degree of co-operation that exists between them. So far as I am aware, no attempt has yet been made to ascertain, by means of an extensive series of tests, which of these factors is the most important and how their interaction differs with different ages and sexes and different types of disease.

Patho-physiological investigations of the *rapidity of the venous reflux* from the thrombosis-disposed regions of the lower extremities postoperatively have thus been carried out only to a limited extent. FRIMANN-DAHL determined by means of phlebography the emptying-time of perabrodil injected into the vena saphena magna after operation for complaints especially disposing to thrombosis (stomach, gall-bladder, urinary-bladder and prostate-gland operations), and in 1935 he reported 29 cases in which the empty-

<sup>1</sup> For this purpose antiprothrombin (AP) manufactured by Ferrosan, Limited, Malmö, has been used.

ing-time was shown to have multiplied several times during the week after the operation. On the other hand, in 9 cases of operation of a non-thrombosis disposing type (strumectomy, thoracoplasty) there occurred no prolongation of emptying-time. With the help of the fluoresceine method in some 40 cases dealt with in the Surgical University Clinic at Lund in 1944 BJÖRK and STRÖMBECK were able to establish a post-operative slowing of the venous reflux from the lower extremities to the greater circulation even during the first twenty-four hours after the operation, followed each day by an increase which did not reach its maximum until about the seventh day of confinement to bed after the operation. The retardation was greater after operations for gall-bladder affections than after, for instance, sectio alta. The findings pointed to greater retardation among older and fat patients. In operations on the thyroid and for cervical and mammary tumours no retardation of reflux was found, neither in this group nor in patients under 20 years of age. In tests reported in 1940 from the Mayo-Clinic by SMITH, ALLEN and CRAIG, natriumcyanide was used and injected into the veins of the lower extremities. The time required for this medium to reach the carotid sinus was indicated by the rapid dilation of the alae of the nose and by a sharp inspiratory gasp. The results show that the time of circulation from the foot to the sinus caroticus is prolonged in the same manner as in our tests, with considerable variations in individual cases, during the days following the operation, while on the other hand the rate of venous reflux from the arm, similarly determined, is not prolonged. The prolongation was somewhat less pronounced than in the material of Björk and Strömbeck. ALLEN and SMITH also found a shortening of foot-carotid-time if thyroid medication was given postoperatively.

Of the *postoperative blood changes* of a great variety of kinds that have been registered, most attention has of course been paid to those that might have some connection with the coagulability of the blood. CRAFOORD was of the opinion that larger doses of heparin were required postoperatively in order to produce a certain prolongation of coagulation time than were required in normal cases. Shortening of coagulation time was established by BERGQVIST in 1944, reaching its minimum at the end of 4 hours. Already about the second day, however, the values were again normal. STARUP, working under AAGE NIELSEN at Aarhus, employed a more exact method and established even during anaes-

thetia a reduced coagulation time with continued reduction during the operation. This increase in the coagulability of the blood lasted in some cases only a few hours and in others up to 4 days after the operation. He found no parallelism between this lowering and the empirically-discovered susceptibility to thrombosis in different types of operation and in different age-groups. Even if the effect of the operation on coagulability is counteracted by small doses of heparin during and after the operation, the liability to thrombosis is not prevented (STARUP). By a method adapted to clinical use BORGSTRÖM has investigated the post-operative variations in the fibrinogene content of the blood in a large number of patients. In practically every case he finds a reduction in the fibrinogene index during the operation and later on an increase which is maximal on the first and second days after the operation. This post-operative increase seems to be somewhat lower in children than in adults, but it is the same after thrombosis-disposing operations such as affections of the gall-bladder as after strumectomies which are usually not followed by thrombosis. The increase is independent of loss of blood, the method of anaesthetizing, or the type of operation, and would seem to be connected with the injury to the tissues caused by the operation.

The changes which are known to occur postoperatively in the coagulant condition of the blood obviously throw no light on the characteristic location of thrombosis in the venous tract or on the tendency of certain operations to produce thrombosis. — The same is evidently valid for the postoperatively increased sedimentation rate and the intravascular aggregation of the erythrocytes (KNISELY et al.).

The third factor conducive to thrombosis, *endothelium lesion*, does not for the present lend itself to investigation as do the previous two factors on clinical material liable to thrombosis. In the formation of local thrombosis in the operative field this factor may be regarded as active but its effect is highly problematic in causing remote thrombosis.

Briefly it may be said that what we know so far about the *retardation of the blood stream* during the postoperative period of liability to thrombosis in various types of operation, speaks in favour of this factor being *active in a fundamental and primary causative manner*. In so far as it manifests itself as a shortening of the coagulation time and an increase in the proportion of fibrinogene in the blood, the *change in the condition of the blood would not*

*seem, however, to play any primary rôle, since it does not run parallel with the propensity to thrombosis, but may be regarded as a general causative factor of secondary importance as compared with the factor just mentioned. In view therefore of our avowedly incomplete patho-physiological knowledge we are not inclined to designate anti-coagulant treatment as being causal. This of course does not mean that an artificial lowering of the coagulability of the blood may not constitute a valuable symptomatic procedure, comparable for example with the antiseptic method of the old Listerian system.*

Although more or less theoretical debates of this kind may yield certain criteria concerning the comparative value of different methods for the prevention and treatment of thrombosis, in the last resort it is empirical tests of these methods that must be pronounced decisive. Great difficulties are, however, involved in attempts to establish by clinical-statistical means the effect of measures for the prevention and treatment of thrombosis. In many respects there are deficiencies inherent in the published material. Care must be taken to see that the case-groups are not only sufficiently large to form the basis of a comparison, but are also statistically homogeneous. Comparison of material from different hospitals should be avoided, since local differences in patients, and in the indications and technique of operation, exposure to infection, thrombo-embolic diagnosis of varying effectiveness, are incalculable sources of error. But even a comparison between case-groups from two consecutive time-periods in the same hospital but treated differently may give rise to misleading results, since other active factors may creep in in the course of the years. The most reliable results will be obtained if during the *same period of time* in the *same hospital-department* every other case is treated indiscriminately with one and every other case with another of the methods to be tested. It is needless to say that in a test of this kind carried out on human material a method which is *a priori* less effective cannot be pitted against one which may reasonably be supposed to be better.

With regard to *early ambulation* fairly unobjectionable statistics come to us from BACKER-GRÖNDAHL of Norway. Here a decrease is shown in *thrombo-embolic morbidity* to about  $\frac{1}{3}$  when early ambulation (at the latest four days after operation) is resorted to.

One source of error which must be noted in making these comparisons is that early ambulation is as a rule followed by early



discharge. In the event of thrombo-embolism setting in late, this will certainly not be diagnosed to the same extent as in hospital. It will not quite suffice to suppose that the hospital would have been informed if anything had happened.

MORTEN's obstetric material is also of interest. In each of two parallel departments 10,000 delivery cases were treated simultaneously. In one department early movements in bed were tried, in the other no such bed-exercises and no ambulation before the eighth day. The difference in the frequency of thrombo-embolism was significantly to the advantage of the department in which early movements were practised. It is, however, remarkable that the number of fatal cases was the same (0.05 %) in both departments. In both the treatment in cases of manifest thrombosis was immobilisation.

In 1945 SVEN JOHANSSON submitted from Gothenburg a large statistic which seems to show that since 1937 *mortality* from thrombo-embolism has gone down to about  $\frac{1}{3}$  of its old rate since early ambulation has begun to be applied more and more consistently. Thrombo-embolic *morbidity*, which was the same (0.68 % and 0.67 % respectively) during the 4-year periods 1933—36 and 1937—40, fell, however, during the period 1941—44, when early ambulation was fully applied, to 0.21 %, which difference (like the fall in the mortality rate) is significant. In this material the data are not, however, full enough to enable us to judge of the homogeneity of the different case-groups. FELLÄNDER has published from Örebro a body of material consisting of 25,240 post-operative cases with early ambulation and a thrombo-embolic frequency of 0.73 % together with 0.17 % fatal pulmonary embolism. Similarly BRANDBERG, in 9,549 operation cases with early ambulation, had 0.81 % thrombosis and a death rate of 0.14 % from pulmonary embolism. Both sets of figures may only be compared with other comprehensive Swedish statistics where the frequency of thrombosis is 2.3 % and 2.6 % and the mortality rate lies around 0.36 %—0.38 % (LINDE and WESTBERG).

DAHL-IVERSEN, during the three-year period 1942—45, used early ambulation from the day after the operation and had then 0.58 % thrombosis complication and 0.12 % fatal pulmonary embolism as against 3.5 % and 0.52 % embolism in a body of operation material covering 20 years and published in 1932.

In 1946 LINDVALL reported from the Military Hospital in Boden the result of 3 years' experience of early postoperative ambulation

applied with remarkable energy. Thus after all abdominal, gynaecological, hernia and genital operations the patients got up in 1 or 2 days. Even peritonitis cases left their bed after 2—3 days. After prostatectomy the patients sat up already on the day after the operation. As controls the experience of the 8 years 1935—42 is drawn upon. In this earlier material the frequency of fatal embolism was 0.15 %, whereas during the period when early ambulation was applied no fatal embolism occurred in 6,318 operation cases. The difference is striking. This material gives no information about morbidity from thrombo-embolism. WESTERBORN, who has long been using early movements in bed combined with early ambulation, has by means of this method had a low rate of thrombosis morbidity since 1931, viz. 0.56 % and 0.59 % respectively and a frequency of fatal pulmonary embolism of 0.13 %. Here already it may be pointed out that the mortality in pulmonary embolism among the diagnosticated cases of thrombo-embolism in these statistics, *e. g.* Westerborn's, is about 22 to 23 %, which is of interest in comparison with Bauer's case-treatment with a rate as low as 0.65 %, to which the writer will later revert.

With regard to the statistics cited, especially those of BACKER-GRÖNDAHL, DAHL-IVERSEN, LINDVALL and MORTENS, there would seem to be no doubt that early ambulation constitutes an effective means of reducing the frequency of thrombo-embolism in post-operative material. What is meant by early ambulation is not quite clear. Later than about the 4th day after the operation we cannot quite reckon on gaining the desired full effect. With regard to the frequent occurrence of venous thrombosis in the calf muscle — FRYKHOLM found it in 39 out of 42 cases investigated — leg movements, such as WESTERBORN recommends, will be effective with somewhat delayed ambulation. There is reason to hope that the method may effect a reduction of mortality to at least  $\frac{1}{2}$ — $\frac{1}{3}$  of the old rate. Those who give the method a trial are surprised to find how well the patients — once the ice has been broken — stand up to it. Intestinal function is sooner restored, subjective recovery is more rapid, and the beds in the department are more effectively used. The method would seem to be the best one so far for controlling the retardation of venous reflux in the thrombosis-disposed area. Its disadvantage lies in the fact that it is difficult to apply in a number of cases (fractures, physically weak patients, sensitive individuals, etc.). It will not entail any increased

risk of rupture in laparotomies. DAHL-IVERSEN found a 2.7 % rate of recurrence after herniotomies. For the rest further reports about postoperative rupture-frequency are awaited.

Of the *anti-coagulant methods* *heparin treatment* was the first to be used. In August 1935 CLARENCE CRAFOORD began, at the Sabbatsberg Hospital in Stockholm, his first series of this kind and reported on the results in June 1937. A month or two later the results of the Toronto-School appeared in print. The Swedish and Canadian experiences show almost unanimously that heparinisation, if it is consistently carried through and used for a suitably long time until the patient is fit to get up again, gives an almost 100 % protection against postoperative thrombotic complications. Criticism has been put forward especially from Danish quarters. Thus AAGE NIELSEN of Aarhus treated a rather large body of material (285) in accordance with Crafoord's scheme postoperatively without any protective effect at all. Nielsen's doses were, however, smaller than Crafoord's. Early ambulation evidently did not occur in these early case-groups for heparin-treatment. OLOVSSON's method — doses of 50 mg twice the day from the day after the operation until the patient gets up again — seems prophylactically to give relatively good protection and with his special type of needle it may be well carried out without causing too great trouble. Early ambulation has not been used in his series. The resulting protection is, however, less complete than that given in Crafoord's reports. OLOVSSON's method is said to be in use now only in isolated cases.

The greatest disadvantage of heparin treatment would seem to be the tendency to haemorrhage, and the writer will presently return to this in the comparison of heparin with dicumarin treatment. The high cost of treatment with heparin, and trouble with the injections combined with the risk of haemorrhage have led to a general discarding of heparinisation as a method of prophylaxis.

*Prophylaxis with dicumarin* seems to have been introduced into the history of medicine by BINGHAM, MEYER, POHLE in Madison, Wisc., U. S. A. January 1941. Their observations were published in October 1941. LEHMANN in Gothenburg has independently been studying its use since the autumn of 1941. LEHMANN presented his first clinical results in the Swedish Surgical Society November 1941. In 1943 he reported his first 170 cases of dicumarin-prophylaxis with only 1 case of thrombosis and 1 of pulmonary embolism but none fatal. In 1945 BRUZELIUS was able to

report from the Lund Clinic 1,448 cases treated postoperatively (Nov. 1941 to April 1944) with dicumarin. In the same year BARKER, CROMER, HURN and WAUGH reported from the Mayo Clinic 1,000 operation cases, treated with dicumarin, most of them being strongly disposed to thrombosis, and among these there was only one case of death from thrombo-embolism. In 1947 BRUZELIUS has produced an extended body of material from Lund, comprising another whole year and totalling 2,182 cases operated on during a period of  $2\frac{1}{2}$  years ( $^{21}_{10}$  1942— $^{20}_{4}$  1945).<sup>1</sup> During this time the frequency of thrombo-embolism at the Clinic has gone down to 1.6 % from the earlier figure of 2.8 %, reckoned on the total of cases operated on. If we exclude the operation-groups in which dicumarin treatment could not be given because of the nature of the case (prostatectomies and bone- and joint-operations), the decrease becomes even more marked although certainly not all of the remaining cases received treatment during the dicumarin period, the figures now being 1.0 % and 2.5 % respectively. This comparison has been made over a period of ten years, 1930—39, and therefore before the modern period of controlled fluid balance. The frequency was, however, much the same during the  $2\frac{3}{4}$  years' period 1940—42, when certain changes in these respects had been introduced. It was not until dicumarin was first employed on a full scale ( $^{20}_{10}$  1942) that the reduction took place. These differences in BRUZELIUS' material are statistically significant. During the period of dicumarin-prophylaxis the number of thrombo-embolic cases observed constitutes 32 % and 41 % respectively of the number that could be reckoned on the basis of the two earlier periods (1930—39 and 1940—42) for comparison. The improvement which has probably taken place in the after-treatment and the increasingly early ambulation of the patients, undoubtedly play a certain part in the favourable results that have been obtained. It may, however, be considered as *probable* that essentially *by means of dicumarin treatment much the same decrease in the frequency of thrombo-embolism may be obtained* as other authors have reported *from early ambulation alone*.

The number of fatal cases of embolism also went down during the dicumarin period and then stood at 0.19 % as compared with 0.49 % earlier. It may be observed that of the 13 cases of embolism during the last period of  $2\frac{1}{2}$  years only 1 occurred among the

<sup>1</sup> These investigations have been made possible by liberal grants from the Therese and Johan Andersson Memorial Foundation.

patients prophylactically treated with dicumarin. The other 12 had not received prophylactic dicumarin therapy and most of the fatal cases occurred in the prostatectomy group. The statistics from the Mayo Clinic based on 1,000 cases showed only one fatal, and that an incompletely treated, case. Of these 1,000 cases 379 had suffered from thrombosis or pulmonary embolism earlier, and in about half of them abdominal hysterectomy had been performed. In a body of material of 678 cases from the same clinic thrombosis had occurred during the period 1927—40 in 44 % and fatal embolism in 8 % of the cases!

The difficulty about the clinical use of dicumarin is that it necessarily demands almost daily prothrombin analysis. This constant control is necessary in order to keep the value of prothrombin within the fairly limited therapeutic zone, empirically determined. In Lund we have kept the prothrombin index between 40 and 60, which corresponds almost exactly with the zone between 10 and 30 % indicated by ALLEN. With a prothrombin index higher than this zone-limit the anti-thrombotic effect would be too weak, with lower prothrombin value the risk of haemorrhage is too great. According to our experience there are, however, no fixed values at which the risk of haemorrhage occurs. In BRUZELIUS' 1947 material haemorrhage had set in at 3.3 % in the prophylactic cures, while haemorrhages took place in 11 cases of manifest thrombosis = 6.5 %, treated with dicumarin. For the last year covered by this material the frequency of haemorrhage in prophylactic cases was only 2.1 % without the occurrence of any increase in thrombo-embolism (1.5 % and 1.6 % respectively). Only in isolated cases has there been any question of large haemorrhages. One fatal case of subdural haemorrhage during the use of spinal anaesthesia must be recorded. It is important to note that the *haemorrhages do not always occur at the index-minimum but often not until 1—14 days after this has been reached*. Haemorrhage can therefore occur with a raising index. Deep fluctuations in the curve are dangerous. The best remedy for haemorrhage is blood transfusion. Vitamin K is also effective, and it is not always necessary to have recourse to big doses up to 100—200 mg; a distinct effect can also be achieved with smaller doses, 0.5—10 mg BORGSTRÖM (1948). Particularly is this so with cases that are sensitive to dicumarin, such as operations for gall-bladder drainage, ileus cases, colostomy cases, and others. Cases of mammary tumours are on the other hand less sensitive.

A comparison between early ambulation, heparin and dicumarin as prophylactics for thrombo-embolism gives, on the basis of these observations, the following results.

Heparin, used in full doses (250 mg per day for an appropriately long time), seems to provide an effective thrombo-prophylactic with a certain risk of haemorrhage but is for practical reasons unsuitable for routine use and may be reserved for isolated specially-disposed cases. Both early ambulation and dicumarin treatment have been reported to give a reduction in the frequency of thrombo-embolism to at least  $\frac{1}{3}$  of that in the material for comparison from earlier periods. Because of the difficulties of comparing different sets of statistics it has hitherto not been possible to decide the preference between the two last-named methods.

In order to clear up these points, as was said by way of introduction, the Surgical University Clinic at Lund arranged during the year 1946, a therapeutic experiment on a large scale. Since during 1945 early ambulation had come to be applied more and more and in the year of the experiment was intended to take place with ambulation beginning from the second to the fourth day after the operation for the majority of cases, it could not be considered unjustifiable to treat the patients, *alternately*, with ambulation alone and with early ambulation + dicumarin treatment, since, according to previous experience, the prospects of escaping thrombotic complications ought to be the same for both groups. In the course of the year, however, it could be established with a certain anxiety that the frequency of thrombosis seemed to lie somewhat higher among those who had not received dicumarin. It was, however, not possible to get a clear view of the situation before the year had reached its end. The early diagnostics of thrombosis has since the beginning of the forties received particular attention. Pain and early tenderness in the calf according to OLOW and plantar tenderness have been carefully observed among the operation cases in general. Doctors and nurses have been especially on the look-out for this. On the first suspected symptoms of thrombosis and signs of embolism, even of an obscure nature, heparin was immediately given, usually combined with dicumarin, as early therapy. With knowledge of the results obtained by GUNNAR BAUER in the treatment of early abortive thrombo-embolism, in which mortality reached only 1.8 % as against 18 % in earlier material (about which more below), it seemed to me justifiable to follow out the experiment.

In order to secure the greatest possible uniformity all the postoperative cases were supervised by the same person, BORGSTRÖM, who also carried out the dicumarin treatment and checked the progress of the experiment, as he had likewise done more than a year previously. With regard to dicumarin treatment as a whole it seems to be a great advantage, in a hospital where several doctors are at work, to place the responsibility for medication on one of them.

During 1946 the number of patients operated on was 2,377. Only 1,831, who were 25 years or more, are here to be counted, since we do not use dicumarin treatment with younger patients. Patients with odd record numbers were given dicumarin (AP), while those with even record numbers did not receive it. The 1,831 operation cases divide up into 940 with odd and 891 with even numbers. Because of the nature of the operation (*e. g.* prostatectomy), difficulties in controlling the bleeding, uncertain functioning of the liver, etc., the dicumarin treatment was considered to be contra-indicated and was therefore withheld in 17.6 % of the patients with odd register numbers and in 17.1 % of those with even numbers. In order to avoid sources of error the operating surgeon, at the end of the operation, was in all cases asked by the anaesthetist whether dicumarin treatment was contra-indicated. The surgeon had no knowledge of the register number. The information obtained was entered in the anaesthesia record, and then on the following day the leader of the experiment administered treatment to those patients with odd numbers for whom dicumarin was not contra-indicated.

The material is fully published by BORGSTRÖM (1947). Among the 940 odd numbers 29 cases of thrombosis were found =  $3.1 \% \pm 0.57$ , and 50 among the 891 even numbers, or  $5.6 \% \pm 0.76$ . The difference in the frequency of thrombosis between the odd and the even numbers is thus weighed in favour of dicumarin treatment. The difference is statistically very closely significant.

If we study the frequency of thrombo-embolism among those treated with A P and those not treated with AP, the difference is seen to be larger, however, and statistically significant. Of 701 cases given dicumarin treatment 16 developed thrombosis complication =  $2.3 \pm 0.57$ . Among 1,130 who did not receive such treatment, 63 cases of thrombosis were observed =  $5.6 \pm 0.69$ . The difference is  $3.3 \% \pm 0.90$ . Here however, it must be noted that among the cases not treated with dicumarin there belongs a group

strongly disposed to thrombosis, namely 69 prostatectomies which were not included in the second group. They load this group unfairly, but this is partially balanced by the fact that 89 goitre-patients who did not develop thrombosis were not given dicumarin because of their slight disposition to this complication. With both prostate and goitre cases excluded the difference between odds and evens is statistically significant in favour of the odds, who clearly showed a lower frequency of thrombosis.

If we reckon the frequency of thrombosis in men and women we find that, putting aside cases of prostate and of goitre, the frequency of thrombosis is the same among men who have received dicumarin treatment as among those who have only had early ambulation. In women dicumarin treatment gives, however, as compared with early ambulation, a lower thrombosis frequency, statistically significant. On what this difference between the sexes depends we cannot at present tell.

*Fatal pulmonary embolism* did not occur among those who received dicumarin treatment. On the other hand it did occur in 4 cases among the odd numbers, all of which did not receive dicumarin. Among the operation cases with even record numbers, which did not therefore receive dicumarin, three were fatal embolic cases. The distribution according to kinds of operation, patients' ages and degree of early ambulation is approximately the same for both odd and even numbers. Prostate cases constitute, as already stated, an exception.

The results of this 1946 experiment at the Clinic seem clearly to show that *by means of consistently applied dicumarin prophylaxis and early ambulation simultaneously, at least with women, results can be achieved which are better than those obtained by early ambulation alone.*

When we try to judge the results of the new methods for the treatment of manifest thrombosis and embolism, difficulties of a diagnostic nature arise. If a massive phlegmasia alba dolens occurs, there can of course be no doubt about the diagnosis. Neither are the classical pulmonary-embolisms with sudden gripping pain, effect on the circulation, and accompanying hemoptysis, specially uncertain from the point of view of diagnosis. But from these clear stages of thrombo-embolism there is a progressive chain with increasing indistinctness of symptoms, until finally a limit can be reached when it is impossible to be sure whether we have to do, for example, with the spraining of a muscle in the calf or with a



rheumatic or pleuritic pain in the breast or with thrombo-embolism.

BAUER has rendered great services in showing how, by means of phlebography, this uncertainty can be eliminated in the majority of cases. By this method he has sought to give a more scientific foundation to the discussion of the therapeutic activity of anti-thrombotic measures. On the appearance of pain or tenderness in the calf, uncertain rise of temperature, etc., phlebography was carried out, BAUER and HELLSTEN were able to confirm their suspicion in  $\frac{2}{3}$ — $\frac{3}{4}$  of cases. In their cases the clinical course of events later confirmed the X-ray diagnosis. Bauer's phlebography was carried out with the patient in a horizontal position. Against this procedure objections have been raised by LINDBLOM, KJELLBERG, LÖFSTEDT, and from Finland by SULAMAA, who recommend a vertical position of the under-leg. LINDBLOM has shown that the heavy contrast, with horizontal leg-position and the ray directed vertically, can form itself into a sediment in the posterior parts of the veins in the under-leg and there simulate a defect. KJELLBERG has further made clear that rather large venous tributary discharge into the deep veins of the under-leg gives so strong a dilution of the contrast injected from below that defect-like pictures may arise. In 1945 BAUER answered this criticism, and insisted that with sufficient experience and with the use also of horizontal ray-direction with the under-leg in a horizontal position these sources of error can be avoided. The possibility remains, however, that a thrombosis may start in the upper part of the femoralis region, perhaps from the adductor veins, as FRYKHOLM holds, or from the prostata or uterine veniplexus. FRYKHOLM has found such high thrombotization with free peripheral veins in 2 out of 42 legs that have been subjected to careful post-mortem.

Irrespective of these sources of error it must be remembered that, thanks to a more efficient diagnostic method, it should be relatively easier than before to establish the presence of thrombosis. ALLEN reports that about half of all the middle-aged and elderly people who die after varying periods of confinement to bed have thrombosis of the deep veins of the leg. Obviously we cannot quite simply compare a thrombosis-frequency obtained by a highly developed diagnostic (*e. g.* phlebography, post mortem) with the frequency figures based on the old clinical symptoms. The fact must not be overlooked that a large number of early cases of thrombosis went unobserved in older days and perhaps

still go unobserved and that not all have manifested themselves, at any rate not during the time spent in hospital. With regard to the mortality rate from fatal lung embolism among cases diagnosed as thrombotic the figures must of course vary with the type of thrombosis diagnosed.

Besides in the examination of a method the whole material must be presented, and not alone the part that has been subjected to treatment with, for example, heparin or dicumarin. Fatal cases that develop too rapidly to be subjected to medical treatment ought to be included in statistics designed to show the effect of the remedy in question. Otherwise the comparison will not be accurate. BAUER's beautiful series of over 9,000 operations included no fatal embolic case. No embolism of an unexpected nature took place. This is the result not only of early heparin treatment and a lucky chance but probably of a more and more fully developed thrombosis prophylaxis by means of early ambulation. According to what BAUER reports to me, his operation cases now leave bed as a rule on the day, and at the latest within two days, after the operation. The thromboses that afterwards occur can, if diagnosed early, be checked by the early heparin-treatment. Hence the excellent results — viz. 0.65 % mortality reckoned on the whole body of thrombosis occurrences at the hospital.

In ZILLIACUS' statistics for 1940—44 from some Swedish clinics thrombosis symptoms were lacking in 84 % of the 161 cases of fatal pulmonary embolism. It is possible that many of these cases of thrombosis could have been diagnosed by a more careful clinical examination.

In Lund BORGSTRÖM has evolved a relatively simple laboratory method which, he considers, enables us to prognosticate thrombosis under formation. He follows postoperatively the *course of the fibrinogen index curve* from day to day and believes that there emerges a characteristic picture when thrombosis is about to set in.

*Early ambulation as the only therapeutic method* is used more seldom in cases of manifest thrombo-embolism. ANDRÉ CHALIER of Lyons reports in 1945, however, that in several thousand operations covering the last 17 years he has been using very early ambulation, preferably on the day after operation, at any rate before the 5th day, and that on the first appearance of thrombosis he has intensified the ambulation and walking exercises. By means of this abortive treatment he has never experienced fatal pul-

monary embolism. No figures are given, however. SÖRENSEN reported from Aage Nielsen's clinic in 1943 one hundred thrombo-embolic cases, which had *alternately* received and not received heparin. All of them were made to get up as early as possible and to perform early movements in bed. It is stated that distinct improvement in the condition of the patients was obtained as compared with the older more immobile treatment, but that the results were the same for those thrombo-embolic patients who had received as for those who had not received heparin treatment. The daily doses of heparin in this series were smaller than those given by BAUER, namely 260 mgm. for the first 11 and 500 mgm. for the subsequent 39 cases. Neither did DAHL-IVERSEN consider heparin to be the fundamental thing.

*Anticoagulant treatment with heparin in the case of manifest thrombo-embolism* would seem to have been introduced by MURRAY and BEST in 1938. As early as 1940 MURRAY was able to report 72 cases that had been treated, with one fatal case of embolism. CRAFOORD reported similar experiences in 1939. In 1940 G. BAUER began his well-known abortive treatment, and it is especially his experiences, recounted in a number of publications, that have attracted attention. During the 6-year period 1940—46 there occurred in this department 154 cases of thrombosis with one fatal case out of 19,898 admitted. In addition to these nosocomial thrombosis cases 104 were admitted from other quarters, of which 2 died. Altogether, therefore, 258 cases of thrombosis occurred with 3 fatal cases of pulmonary embolism. The death rate for a 10-year period in the same hospital before the introduction of heparin was 20 per 10,000. During the 6 years of heparin treatment there has occurred no fatal instance of pulmonary embolism in more than 9,000 operation cases.<sup>1</sup> During this 6-year period prophylaxis by means of early movements and early ambulation has been more and more strictly enforced. BAUER in reply to an inquiry informs the writer that at the beginning of the period the hernia patients were kept in bed one week, the laparotomy patients approximately the same time and the appendectomy cases 3—4 days. At the end of the period the patients operated on leave bed as a rule on the day, and at the latest within two days, after the operation. The importance of this early ambulation as prophylactic has just been pointed out. As a direct proof of the part played by

<sup>1</sup> BAUER in Sept 1947 reports about 12,000 operations during the last seven years without any single death from post-operative embolism.

heparin in achieving these good results it may be stated that no extension of a calf thrombosis to the thigh has occurred in Bauer's cases.

In post-hospital investigations of 184 thrombosis cases, which were diagnosed before the extension to vena poplitea had taken place, and which had not shown any propagation during the hospital period, such symptoms as swelling, induration or pains were lacking after an observation-time of at least two years. 72 who had not received heparin treatment until phlegmacy had developed showed on the other hand in half the cases swelling and incipient induration already after 3—5 years.

ZILLIACUS' collection of a comprehensive set of statistics from some 20 Swedish clinics 1940—45 shows that 214 thromboses conservatively treated resulted in fatal embolism in 9.4 % of cases and in extension to the other leg in 31 %. Of 576 cases of thrombosis specifically treated (heparin or dicumarin) the process remained confined to the under-leg in approximately every other case. Fatal pulmonary embolism was found in 3 = 0.5 %. Extension to the other leg in 1.6 %. 154 cases treated with heparin with extension to the thigh had leg ulcers in 7.1 %, while 130 under-leg thromboses treated with heparin had leg ulcers only in 0.8 %. If the process during or before heparin treatment spread to the thigh, there was no difference in the frequency of post-thrombotic trouble between the cases treated according to the old method and those specifically treated. There occurred, however, bilateral trouble in 3 of the specifically-treated cases but in 39 of the conservatively-treated ones.

The use of *dicumarin* for the treatment of manifest thrombosis has been less fully tried out. As a disadvantage of this drug has been mentioned its slower influence on the coagulation conditions of the blood and thereby its late effect on the developing thrombotisation process. Pure dicumarin treatment has been presented in BRUZELIUS' material. In 1947 he reports 168 cases of thromboembolism for a period of  $2\frac{1}{2}$  years treated with dicumarin only. The mortality was as low as 0.6 % or as 3.3 %, according to how we interpret the cause of death. The corresponding percentage for the 10-year period 1930—39 was 17.8, in which figure all thromboses have been included.

Progress of a thrombotic process localized to the under-leg was not observed, on the other hand pulmonary embolisation occurred during effective dicumarin-treatment in 5 of 113 cases.

The *risks from the use of dicumarin* have, in our experience, been exaggerated. It may be granted that dicumarin is a toxic element foreign to the body, and that in doing its work it causes slight inhibition of the prothrombin-producing function of the liver. With our cautious dosage and careful observation we have, however, found no damage to the liver. The drug ought, however, to be avoided when there is reduced functioning of the liver or risk of obstruction of the outflow of urine as after Coffey's operation. Experiments on animals show a higher degree of sensitivity to dicumarin after ureter ligation. Heparin is, on the other hand, a physiological substance which, however, is used in non-physiological doses. The *risk of haemorrhage* is common to both drugs. It may occur *in any anticoagulation treatment*. The coagulation mechanism is upset pulsatingly and intermittently in the case of heparin treatment but more uniformly in the case of dicumarin. When using the latter drug the prothrombin values can be maintained for day and night within the therapeutic zone and do continuous effect, but of course also, if they fall too low, in a more intensive and continuous manner they may create the conditions for haemorrhage. The effect of heparin exceeds soon after the injection whatever is needed for therapeutic purposes but decreases quickly, whereupon an interval with normal coagulation follows. This difference between heparin and dicumarin is existing both in treatment and in prevention. If dicumarin is used for prevention soon after the operation when the risk of haemorrhage is greatest and heparin only for therapy several days later, when the risk of haemorrhage is in itself less, it is also natural that the possibilities of haemorrhage should seem greater in the case of dicumarin. This is not due to the drug as such but to the way in which it is used. With knowledge of these facts and with sufficient practical experience it will be found possible to avoid, with considerable certainty, haemorrhage complication. BRUZELIUS had 4.4 % haemorrhage in the prophylactic material of the first 1½ years and 2.1 % in that of the last year (902 prophylactic cases). In cases of manifest thrombosis the frequency of haemorrhage fell from 9.7 % in the first period to 0 in the last (55 cases). During the year 1946 the frequency of haemorrhage was 1.6 % in 701 patients prophylactically treated with dicumarin and 0.5 % in 1,130 operated cases without dicumarol. With regard to the use of dicumarin it must be recalled that, as BRUZELIUS has pointed out, haemorrhage can occur after the dicumarin has lessened its

effect so that the protrombin curve has already left the haemorrhage zone.

In weighing one against the other the anticoagulant drugs in therapeutic use for manifest thrombosis, it ought first to be remembered that, as BAUER and his collaborators have shown, heparin can stop the development of a diagnosed under-leg thrombosis and that encroachment on vena poplitea with an accompanying tendency to swelling can be effectively forestalled. In this way, however, we do not get at the cases of thrombosis that do not start in the under-leg. According to BAUER these constitute about 2 % and according to RÖSSLE about 7 % of all cases of thrombosis. Fatal pulmonary embolism can, like a bolt from the blue, surprise not only the negligent diagnoser but also those who watch daily over patients that have been operated on and who are especially on the look-out for symptoms of under-leg thrombosis. For such cases there is no treatment. According to ALLEN an early thrombosis must be stopped within 24 hours if the risk of embolism is to be avoided. Dicumarin cannot produce so fast a coagulation effect but must here be supplemented by heparin, which in this respect is clearly superior. In order to obtain the valuable continuous effect of dicumarin for the whole twenty-four hours, the dicumarin should be joined up at the same time and be given an opportunity of developing its effect while medication with heparin is gradually finishing off its work.

Concerning the *late results of therapy cases treated with dicumarin* no investigations, so far as I know, have yet been undertaken. A follow-up examination is recently made by WELANDER of 98 patients treated with dicumarin at the surgical clinic in Lund. "After a period of 2—4 years of observation 76 % of 42 patients with thrombosis of the calf were completely free from symptoms. Among the patients with post-thrombotic sequelae, the symptoms were generally mild. Only one patient in this group suffered from a leg ulcer.

Most of the 20 patients, among whom the thrombosis had extended to the thigh, suffered from discomfort in the leg (75 %). Leg ulcers were observed in 15 %." Thus the late results not seem to be quite as good as when heparin was used.

In conclusion it may be said that both heparin and dicumarin have their advantages and certain disadvantages. It would seem as if the most effective result in the anticoagulation treatment of manifest thrombosis is to be attained through a combination of the two.

Finally the writer should like to outline the plan which, with the existing diagnostic and therapeutic methods, seems to him most capable of giving the greatest protection against the appearance of thrombosis and against the development, extension, and embolisation of a thrombosis that has already occurred. 1) *As prophylaxis the fundamental and most important thing is early ambulation*, preferably on the first day, and at the latest 2—3 days, after the operation. 2) This early ambulation ought if possible, especially in the case of women, to be *supplemented by dicumarin prophylaxis*, beginning on the day after the operation in order that, during the whole period of healing until the patient is fully mobile again, the prothrombin may remain in the therapeutic zone (index 40—60 = protrombin percentage 10—30). Such dicumarin prophylaxis can be instituted in about five of six post-operative cases and is contra-indicated in cases of liver injury, in cases of special tendency to haemorrhage and incomplete control of bleeding from the wound, and in certain renal affections. 3) *Early diagnosis of thrombosis complications* must be learnt and developed by doctors and nurses, so that *early therapy with heparin and dicumarin at the same time* may be begun on the distinct appearance of thrombosis but also when there is sufficient ground for suspecting that such early thrombosis may exist.

In my opinion, if the tendency to thrombosis is sufficiently great in a body of clinical material, neither of the two prophylactic methods (early ambulation and anticoagulants) should be dispensed with, nor should early therapy with *both* of the anticoagulants be done away with. All three are equally necessary and it is relatively meaningless to weight them against one another.

In this paper the *surgical* prophylaxis and the *surgical* therapy of thrombo-embolism have been dealt with. The same principles are applicable to internal-medical, obstetric-gynaecological, ophthalmological and otological cases. Perhaps it is in internal-medicine most of all that attention ought to be paid to the injuriousness of confinement to bed as a factor strongly disposing to thrombosis. Confinement to bed can certainly be done without to a far greater extent than is generally thought. Those surgeons who have been converted to looking upon early ambulation as a valuable preventive measure would like to see their faith shared by their internal colleagues. As an important adjuvant the anticoagulation methods too should be used in internal medicine.

## Summary.

The retardation of venous reflux from the thrombosis-disposed areas is a factor of fundamental and primary importance in the development of venous thrombosis. Early movements and early ambulation is the best method known at present time for causative prevention of thrombosis.

Anticoagulants — and for practical reasons in the first place dicumarin — may have a valuable auxiliary prophylactic effect. So the simultaneous use of dicumarin and early ambulation gives better results than early ambulation alone, at least with women. Treatment of manifest thrombo-embolism with heparin, supplemented by dicumarin, started as early as possible and followed by early raising seems to give the best guarantees for good immediate and late results.

Venous interruption as a prophylactic or therapeutic measure is not concerned with in this study.

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## Determination of Acid and Alkaline Phosphatase in Blood-serum and the Value of this Method of Investigation in the Diagnosis of Cancer Prostatae.

By

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Stockholm.

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Phosphatase is an enzyme having the power to catalyze the hydrolysis of practically all monophosphoric acid esters, both aliphatic and aromatic. Phosphatase is found in the vegetable and animal kingdoms. According to the hydrogen ion concentration required by the enzyme for the exercise of its maximum effect, one distinguishes between alkaline and acid phosphatase. As regards phosphatases of clinical importance, the alkaline generally have an optimum of pH 9—10 and the acid of pH 4—6.

ROBISON (1) in 1923 showed the occurrence of alkaline phosphatase in bone and bone-forming cartilage. In cases of generalized osteopathy, such as active rickets, osteitis fibrosa generalisata (hyperparathyreodism), osteitis deformans (Paget's disease), generalized osteoporosis, osteomalacia, malignant tumors metastasizing to the osseous system, Gaucher's disease, or extensive fractures, the enzyme seems to flow out into the blood and is found in considerable amounts in the blood-serum. A phenomenon the cause of which is not yet known is the increase of the alkaline phosphatase activity found in blood-serum of icterus case with relative obstruction of the bile-ducts. See ROBERTS (2), ARMSTRONG, KING and HARRIS (3).

In 1934 BAMANN and RIEDEL (4) isolated acid phosphatase with an optimum pH-value of 4.5—5.0 from the spleen and liver of pigs, and DAVIS (5) isolated an acid phosphatase with an optimum pH-value of 6 from spleen and red cells. KUTSCHER and WOLBERGS (6) in 1935 made the important discovery that the prostate tissue is very rich in acid phosphatase. GOMORI (7) in 1941 showed that the acid phosphatase in the prostate was localized in the acinous epithelium of the gland.

By determining the optimum pH-value of the different acid phosphatases, the rate of hydrolysis in their action on different substrata, and the dissociation constant of the enzyme-substrate compound, inhibition in the presence of fluoride ions (8), ethyl alcohol (9) or formalin (10), it is possible to separate them from the other.

The acid phosphatase in the acinous epithelium of the prostate is not formed until after sexual maturity. By injecting an androgenous hormone into sexually immature Rhesus monkeys, GUTMAN and GUTMAN (11) evoked the production of a prostatic secretion with a high enzyme activity. According to A. B. GUTMAN (12), prostatic cancer-cells likewise generate acid phosphatase. After metastasis the cancer-cells retain this capacity for forming acid phosphatase; see GUTMAN, SPROUL and GUTMAN (13). The blood-serum normally has a very slight acid phosphatase activity, whereas the activity of the prostatic fluid is 50,000—100,000 times greater. It is thus evident that merely an efflux of a slight amount of prostatic secretion into the blood-stream is required to increase the acid phosphatase activity in the blood-serum beyond normal. This amount may be estimated at less than half a milliliter. Should the growing prostatic cancer-tissue penetrate into the lymphatic channels or blood-stream, the cancer secretion may possibly leak out into the circulating blood, thus increasing there the amount of acid phosphatase.

With the intention to show this increased activity of the acid phosphatase in patients' blood with metastases of cancer prostatae, various methods for its determination have been elaborated. The procedure indicated by KING and ARMSTRONG (14) has served as a basis for a number of modified methods in which phenyl phosphate is used as a substratum. The amount of phenol liberated in the hydrolysis is colorimetrically determined.

The phosphatase unit according to KING and ARMSTRONG is defined as the fermental activity that has liberated 1 mg phenol on

1 hour at pH 4.9 and  $+37^{\circ}$  C. The literature on this subject is rather confusing, as different units are given as a gauge of the phosphatase activity (*e. g.* KING and ARMSTRONG, KAY, JENNER and KAY, ROBERTS, BODANSKY, BUCH and BUCH, etc.). It is therefore of great importance, in connection with the investigations, to indicate the unit adopted and the limits of its normal value. Certain methods in which other phosphoric acid esters have been used as a substratum have lately been described. HUGGINS and TALALAY (15), for example, used sodium phenolphthalein phosphate. This method has been tested by us but rejected, on the ground of its lack of proportionality between pigment formation and enzyme activity. Another method is based on the hydrolysis of p-nitrophenolphosphate, where the amount of liberated p-nitrophenol is directly determined colorimetrically after acidification of the reaction mixture (16).

In 1938 GUTMAN and GUTMAN (17) published the first investigation into acid phosphatase in cases of cancer prostatae. Since then several similar investigations have been published, especially in U. S. A. In Sweden, BORGSTRÖM (18) in 1946 reported an investigation on that subject. All these investigations seem to show that in a large number of cases there is an undoubted, and often marked, increase of the acid phosphatase activity in the serum of patients suffering from metastasizing cancer prostatae. Such an increase is rarely found in healthy subjects or in patients with other diseases in or outside the prostate, including prostatic cancer that had not yet given rise to metastases.

HERGER and SAUER (19), in a work of 1941, state that values of over 3 units (KING-ARMSTRONG) for acid phosphatase activity are pathological. Their series comprise 69 cases of prostatic cancer, 3 cases of suspected cancer prostatae and 28 control cases. They found that 94 per cent of the cases with undoubted or suspected metastases and 16 per cent of the cases without metastasis showed pathological values. It should be noted, however, that the three cases with suspected prostatic cancer and 18 per cent of the control cases all showed values above normal. In a later report on a larger investigation, comprising 147 cases of cancer prostatae and 283 control cases, the same authors (20) express the view that phosphatase values of over 4 units (KING-ARMSTRONG) should be regarded as pathological. In this series 91 per cent of the 47 cases with undoubted or suspected metastases showed higher values, whilst 13 per cent of the other cancer cases and 7.5 per cent of the

control cases showed a rise. SULLIVAN, GUTMAN and GUTMAN (21) published in 1942 an extensive investigation, comprising no less than 200 cases of cancer prostatae and 685 control cases. They designate values of over 3 units (KING-ARMSTRONG) as pathological. Such values were shown by 85 per cent of 130 cases with metastasizing prostatic cancer, where the diagnosis was roentgenologically verified. Among the other cancer cases 11 per cent showed raised values. The control material had pathological values in 8 per cent of the cases. This material included 75 cases with prostatic hypertrophy and 10 cases with prostatitis, all of which showed normal acid phosphatase values. BORGSTRÖM's (18) investigation of 1946 from the surgical clinic at Lund comprises 20 cases of prostatic cancer, 12 of which had skeletal metastases. Eight of the latter showed phosphatase values of over 3 units (KING-ARMSTRONG), which was designated as the normal upper limit. Two of the 8 cases without metastasis showed raised values. No control material is reported.

As regards the *alkaline* phosphatase in the blood-serum in cancer prostatae, it seems, according to investigations by HERGER and SAUER (19, 20), that it likewise shows an increase in some cases of metastasis.

### Own Investigations.

During the period 1944—October 1947 a large number of patients with different diseases have been examined at the surgical clinic of Karolinska Sjukhuset in respect of acid and alkaline phosphatase activity in the blood-serum. The investigation technique is a modification of a procedure proposed by BUCH and BUCH (22). A unit according to our procedure corresponds to about four units according to KING and ARMSTRONG. In this technique we have introduced treatment of the serum with formalin, whereby any error due to the possible occurrence of acid phosphatase from hemolyzing red cells in the blood sample may be considered eliminated. The object of the investigation was to ascertain the upper limits of the normal value for acid and alkaline phosphatase activity and to determine the value of the investigation technique pro 1:0 in the differential diagnosis between prostatic hypertrophy and prostatic cancer, pro 2:0 in judging these cases of cancer.

## Technique.

The *alkaline phosphatase* activity was determined according to the modification of KING and ARMSTRONG's technique proposed by BUCH and BUCH (22). These authors express the phosphatase activity in half the number of mg phenol liberated from phenyl phosphate by 100 ml of serum in 15 minutes at pH 9.9 and  $+37.5^{\circ}\text{C}$ . The normal values with this technique range between 2—8 units.

The *acid phosphatase* activity was determined with a modification of BUCH and BUCH's technique. The serum was incubated for 30 minutes at pH 4.9 and  $+37.5^{\circ}\text{C}$ . We found that a citrate buffer solution was preferable to an acetate buffer. The substratum solution must be kept separate from the acid buffer solution, as otherwise the phenyl phosphate will be spontaneously split. Two analyses were made, the one with an addition of formalin, the other without it. In this way the effect of the prostatic phosphatase could be distinguished from that of the erythrocyte phosphatase, as the effect of the latter is inhibited by formalin.

1.25 ml citrate buffer

1.25 ml aq. dest.

2.5 ml phenyl phosphate solution

0.25 ml serum

1.25 ml citrate buffer

1.25 ml 2 % formaldehyde (exactly)

2.5 ml phenyl phosphate solution

0.25 ml serum.

The acid phosphatase activity is expressed as half the number of mg phenol liberated by 100 ml serum in 30 minutes at pH 4.9 and  $+37.5^{\circ}\text{C}$ . The normal values with this method lie between 0 and 2 units.

## Clinical Investigations.

The material comprises 600 carefully examined cases.

Table 1.

Control cases .....	94
Hypertrophica prostatae .....	309
Suspected cancer prostatae .....	25
Cancer prostatae without detectable metastases .....	108
Cancer prostatae with undoubted metastases .....	64
<hr/>	
600 cases.	

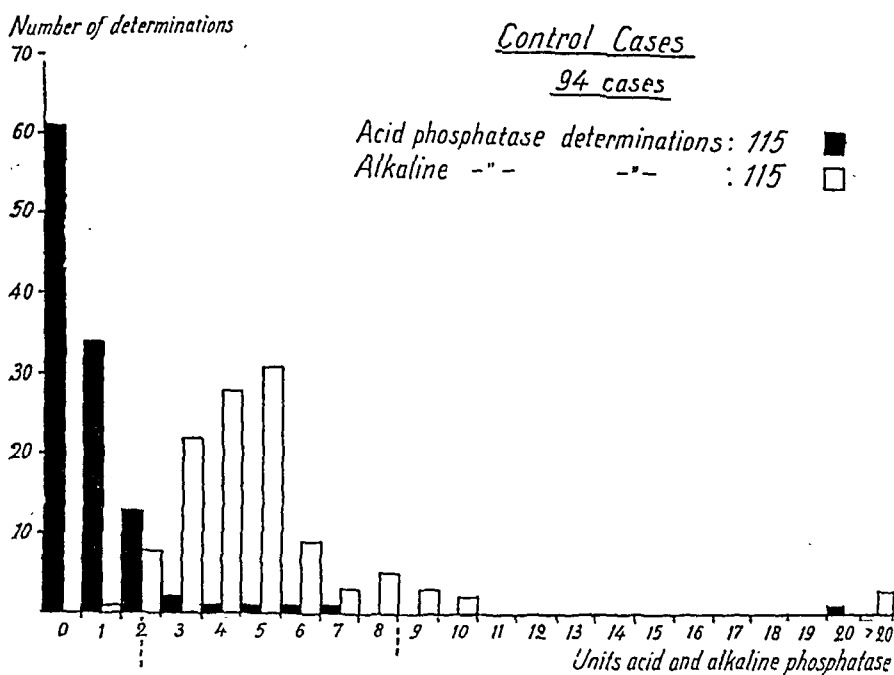


Fig. 1.

The 94 *control cases* were patients suffering from acute or chronic prostatitis, prostatic abscesses, prostatic tuberculosis, infections of the urinary system, renal calculus, bladder-neck sclerosis, bladder tumors or diseases in the skeletal system. 115 determinations of acid and alkaline phosphatase were made in these cases; the values are distributed in the way shown by the diagram in Fig. 1. As we see, most of the values for acid phosphatase range between 0 and 2 units, merely 6 per cent of the determinations being over 2 units, and 17 per cent over 1 unit. If the 6 cases showing values over 2 units are closely examined, it will be found that they consist of a case of lumbago-sciatica with 6 units, where two of the controls afterwards showed 0 unit, a case of chronic cystopyelitis with 3 units and 1 unit, respectively, a case of vesical cancer with 20 units,<sup>1</sup> a case of bladder-neck sclerosis with 3 units, a case of chronic osteomyelitis with 0.7 and 5 units, and a case with chondromatous and osteochondromatous foci with 4 units. The values for alkaline phosphatase are concentrated round 3—5 units, practically speaking in the form of a so-called normal curve and, if the limit is drawn at 8 units, 7 per cent of the determinations will be found to lie above it.

<sup>1</sup> This man has according to his present condition very probably a cancer prostatae.

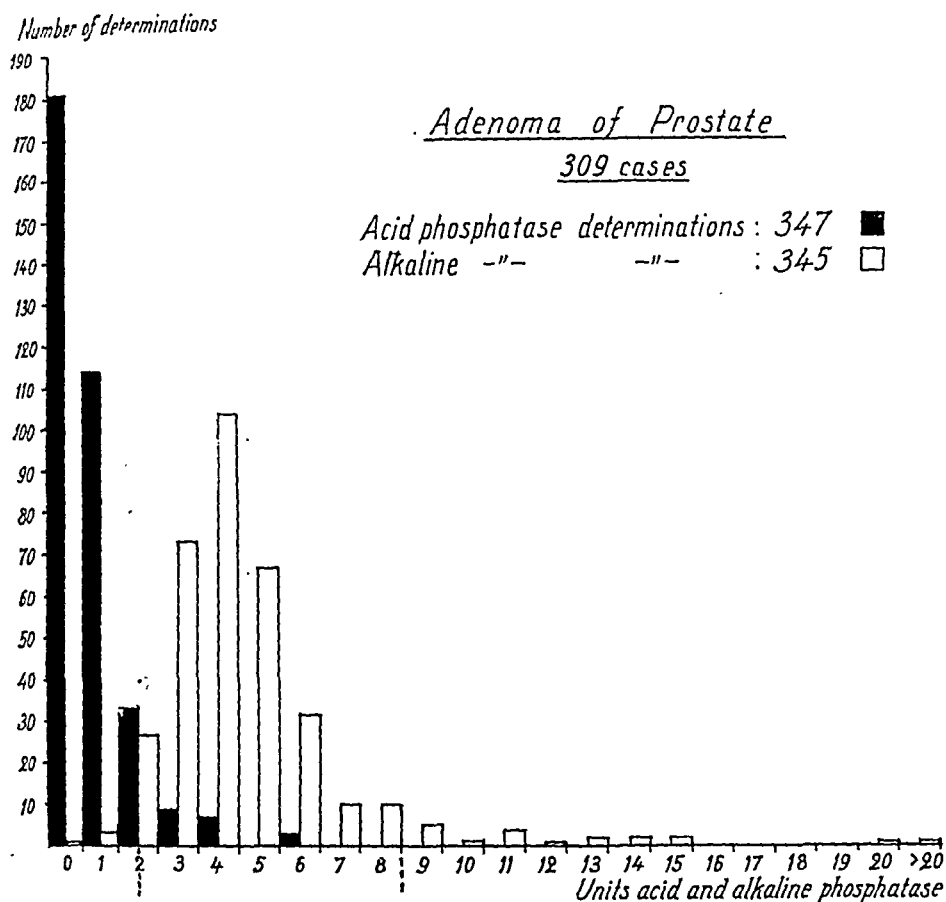


Fig. 2.

In the 309 cases of *prostatic hypertrophy*, 347 determinations of acid phosphatase and 345 of alkaline were made. The diagnosis was verified by histological examination in 231 cases. The distribution of the values for acid and alkaline phosphatase (see Fig. 2) is practically identical with that of the control material; 5.5 per cent of the values for acid phosphatase are over 2 units and 15 per cent over 1 unit. As regards the alkaline phosphatase, 5.5 per cent of the values are over 8 units. In none of the 19 cases with an acid phosphatase activity of more than 2 units was there any clinical, roentgenological or pathologico-anatomical suspicion of cancer. Eight of these cases were subjected to a follow-up examination six months to two years after the first examination and in none of them was there any suspicion of cancer.

The diagnosis in the 25 cases of *suspected cancer prostatae* was made either on the ground of the palpation result or on the ground of the histological examination after electroresection or prostatectomy. One patient had skeletal metastases and the pal-



*Carcinoma of Prostate doubtful*  
25 cases

Acid phosphatase determinations: 30 ■  
 Alkaline " " " : 29 □

*Number of determinations*

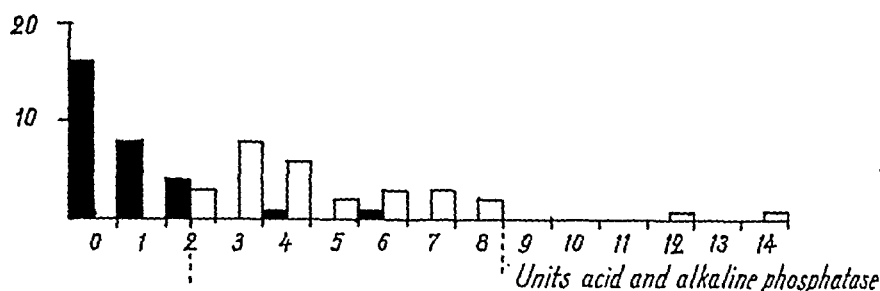


Fig. 3.

pation result arose some suspicion of prostatic cancer; probably, however, it was a case of primary pulmonary cancer. Thirty determinations of acid and alkaline phosphatase were made (Fig. 3), 6.7 per cent of the determinations for acid phosphatase showed a higher activity than 2 units, 20 per cent of them higher than 1 unit. As regards alkaline phosphatase, 6.9 per cent showed an activity of more than 8 units. As we see, the correspondence with the control material is good. The two cases showing a high acid phosphatase activity were those of a patient who died of cancer recti 1 year after the examination, and of a patient subjected in January 1947 to transvesical prostatectomy, the pathologico-anatomical diagnosis having indicated suspicion of prostatic cancer.

In the 108 cases of *cancer prostatae without detectable metastases*, the diagnosis was verified by histological examination in 81 cases, after electroresection or prostatectomy. In three of these cases the histological examination did not show cancer, but the clinical diagnosis was considered certain. X-ray examination of the pelvis, vertebral column and lungs was made in 41 cases, examination of the pelvic skeleton or of the latter and the lungs in 62 cases and of the lungs alone in 2 cases. Three of the patients were not subjected to any X-ray examination, but showed

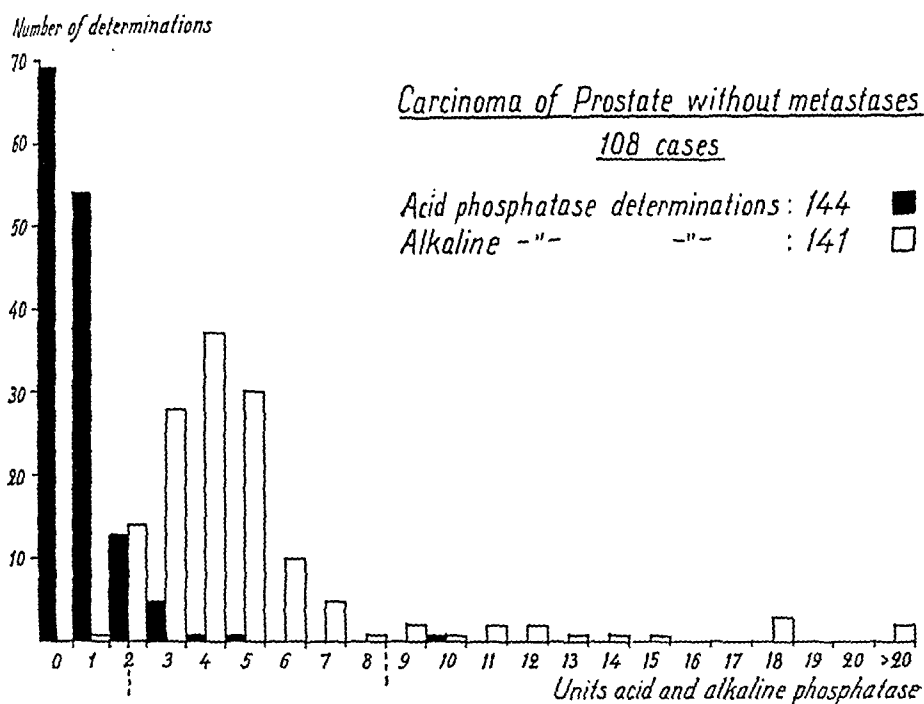


Fig. 4.

no clinical symptoms of metastases. 144 determinations of acid phosphatase and 141 of alkaline were made (Fig. 4). As regards acid phosphatase, 5.6 per cent of the determinations were over 2 units and 15 per cent over 1 unit, thus showing a very good correspondence with the control material. As for the determinations of alkaline phosphatase, 11 per cent were over 8 units. All determinations were made before the institution of any hormone or X-ray treatment.

As regards the 64 patients with *metastasizing prostatic cancer*, the histological diagnosis is positive in 33 cases, negative in 1 case. On the other patients no operation on the prostate was performed. In 59 cases roentgenologically detectable skeletal metastases were found, whereas in the remaining 5 cases the X-ray examination was negative in this respect. Out of these 5 patients, four had metastases in the inguinal lymphatic glands and one showed a liver metastasis. 82 determinations of acid and alkaline phosphatase were made (see Fig. 5). As may be seen from the diagram, the distribution of acid as well as alkaline phosphatase is here quite different than in the previously reported groups. 38 per cent of the acid phosphatase values are over 2 units, 48 per cent over 1 unit. As for the alkaline phosphatase values, no less than 55 per cent are over 8 units. In this group of patients

Carcinoma of Prostate with metastases64 cases

Acid phosphatase determinations : 82 ■  
 Alkaline " " : 82 □

Number of determinations

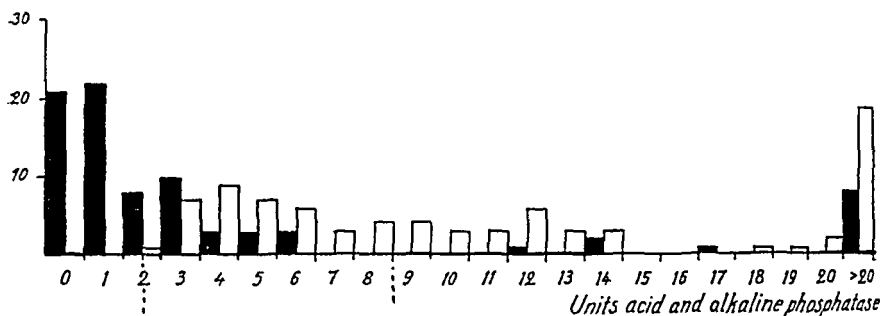


Fig. 5.

too, no hormone or X-ray treatment was instituted pending determination of the phosphatase activity.

### Discussion.

In a biological method of investigation there are always certain sources of error, such as errors in taking samples, direct errors in technique and biological variations. In the application of such a method it is essential if the method should be of any value, that the limit of the normal value is carefully fixed and so chosen that there will be as few pathological values as possible within the control material. In our material all the groups — setting aside metastasizing prostatic cancer — in regard to the determinations of acid and alkaline phosphatase, show well corresponding distribution curves; and if for acid phosphatase we take 2 units as a basis for the upper limit of the normal, only 5—6 per cent of the determinations show pathological values. This deviation may be regarded as satisfactory in a method of this nature. We accordingly consider that the normal limit for acid phosphatase may be set at 2 BUCH and BUCH units (thus corresponding to 8 KING and ARMSTRONG units) and, for similar reasons, that the normal limit for alkaline phosphatase can be set at 8 BUCH and BUCH units.

The principal source of error in the determination of acid phosphatase in the blood-serum is the greater activity that occurs in the event of total or partial hemolysis. Thus, totally hemolyzed blood shows an acid phosphatase activity of up to 40 units. In order to eliminate this source of error we have tested several methods, finally adopting the separation with formalin recommended by ABUL-FADL (10). The erythrocyte phosphatase is completely inhibited, the prostatic phosphatase, on the other hand, quite slightly, by formalin in a certain concentration in the reaction mixture.

The large number of cases with pathological values for acid phosphatase in metastasizing prostatic cancer according to the previously summarized investigations is remarkable, but on closer examination it will be found that, in a considerable number of instances, pathological values occur in the control cases of these investigators as well as in their cases of cancer without metastases. It may moreover be noted that several of their tests are invalidated by sources of error in the form of hemolysis.

From our investigation it may be inferred that in the differential diagnosis between prostatic hypertrophy and prostatic cancer the determinations of acid and alkaline phosphatase are of little avail. In metastasizing prostatic cancer an increase of the acid phosphatase above normal is observable in more than one-third of the cases (in our material 39 %). A normal acid phosphatase value thus does not exclude the possibility of metastases, whereas a pathological value is a distinct indication of their existence. In several cases, thanks to the investigation, metastases had been suspected long before they had been roentgenologically verified. In about half the cases of metastases we observe an increase of the alkaline phosphatase, as a rule simultaneously with the increase of the acidic. This increase of alkaline phosphatase activity in the blood-serum should be regarded as a non-specific reaction caused by alkaline phosphatase liberated from the bone tissue, but may lend some support to the diagnosis.

This method of investigation is thus of rather limited value in regard to the diagnosis of prostatic cancer, but serves as a supplement to the clinical examination. Should acid phosphatase in the blood-serum, on repeated examination, show a pathological value, it is, in all probability, a case of prostatic cancer with metastases; hence, in cases with early skeletal metastases, which are often very difficult to detect with the X-ray, the investigation

may determine the diagnosis. In vesical tumors, especially those at the base of the bladder, where the differential diagnosis is between vesical cancer and prostatic cancer, as well as in cases with skeletal metastases of unknown genesis, investigation of the phosphatase activity may be of great value.

The value of this method of investigation for judging the prognosis in cases of prostatic cancer, its value in the control of the treatment as well as the question whether there is any connection between acid phosphatase activity and the degree in which prostatic cancer can be differentiated, are matters that will necessitate further investigations.

### Summary.

In a material comprising 600 cases the acid and alkaline phosphatase activity in the blood-serum was determined. In order to rule out the effect of other acid phosphatases (such as those from hemolyzing red cells), most of the analyses were made in the presence of formalin in a concentration of 0.16 mol per liter. The normal upper limit for alkaline phosphatase was found to lie at 8 units (BUCH and BUCH) and for acid phosphatase at 2 units (BUCH and BUCH). The cases of hypertrophia prostatae, suspected cancer prostatae and cancer prostatae without detectable metastases showed normal values both of acid and alkaline phosphatase, compared with the control material. In 39 per cent of the cases of cancer prostatae with metastases the acid phosphatase activity was raised. As regards the alkaline phosphatase in this group, it was raised in 58 per cent of the cases.

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## Abdominal Wall Varices Secondary to Thrombosis of the Iliac Vein.

By

OLOF OLSSON.

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In the summer of 1947 a patient presented himself at the hospital with complaints of varices on the lower part of the abdominal wall and of both legs. The first impression gained was that of a caput medusae but a further study of the history and status disclosed that there here was the question of compensatory collaterals to an obliterated iliac vein.

The patient was a 28-year-old woodsman from Värmland who at the age of 14 had been treated at Sunne cottage hospital under the diagnosis appendicitis acuta gangrenosa + thrombophlebitis crur. sin. (vena femoralis). After the appendectomy he was in bed for 10 or 11 days but had the day after being allowed to get up increasing pains in the left groin. The next day the pain spread to the lower abdomen, coincidently with the onset of a swelling of the left leg, wherefore he was again confined to bed. After bed rest for 3 to 4 weeks he was discharged and was at that time free from discomfort from both the abdomen and the leg, but after the lapse of a few weeks he observed varices below the navel. These have during the course of time increased successively but have not given him other trouble than a feeling of discomfort. During the last 2 to 3 years he has had varices of the legs, thus especially the left leg, which has been moderately swollen and has felt heavy at prolonged stationary work. He was treated by means of injections for the varices of the legs one year ago.

At examination 7. 21. 1947 the varices depicted on fig. 1 were seen, tortuous veins the thickness of a finger, forming a loop up to the umbilicus from the one groin to the other. On the left lower leg there were observed moderate tortuous varices in the saphena magna area and

on the left thigh a distended saphena magna was palpated as far up as the fossa ovalis. The right leg showed only slight saphena magna varices of the lower leg. The legs were not swollen. PERTNIES' test performed with the stasis tube immediately above the knee showed good emptying of the veins in the lower legs. When the abdominal varices were massaged empty and pressure applied to both groins the varices did not become filled, wherefore it could be excluded that the origin to the varices was portal hypertension. On the pressure in the right groin then being released (fig. 2) the varices did not fill up, but as soon as the pressure in the left groin was released it was observed that the blood immediately filled the abdominal varices from the left. It was accordingly obvious that the direction of the flow in the varices was from the left to the right and that the probable origin of the varices was an obstruction in the left iliac vein.

In order to confirm the diagnosis a venography was performed (Dr. LARSSON). The left saphena magna was punctured just above the middle of the thigh, pressure was applied to the abdominal varices and both legs were compressed with large calibre rubber tubes, the right leg at the upper point of the groin and the left leg below the site of the venipuncture. After this 20 ml of 35 per cent Dijodon were rapidly injected and with the patient in the recumbent position 4 views of the pelvic region were taken, the first at pressure of the abdominal varices and the remainder after the release of compression. On the first picture are only seen the contrast filled long saphenous vein and the varices in the left fossa ovalis. On the second (fig. 4) are in addition seen the contrast filled varices of the abdomen between the left groin and the umbilicus, as well as a number of veins adjacent to the pubic region. A large venous branch (at the lower, triangular indicator in the left groin) comes to an end suddenly and is probably the obliterated femoral vein. On the third picture (fig. 3) the veins in the left fossa ovalis and the abdominal varices on the left side have emptied their contrast but now the contrast filled varices of the right side of the abdomen are seen, as well as the right iliac vein and a plexus in the pubic region. On the last picture is seen only a very weak contrast filling of the left iliac vein, a tortuous varix in the right fossa ovalis and some veins in the pubic region. It thus appears from the venography that the blood from the left leg is emptied into the right iliac vein via the large abdominal wall varices and a plexus in the pubic region, and that the left iliac vein is obliterated.

In studying the literature of the last 10 years the author found a case very similar to this (GOOEL).

It was that of a 23-year-old woman who 4 years previously, 6 months after an operation for left-sided congenital dislocation of the hip, had abdominal varices of the same appearance as those in the present case, although the convexity of the varix sinuosity in her case was somewhat below the umbilicus. Her varices had developed successively over a period of 4 years, beginning in the left groin. At operation of the



hip there were not observed any signs of thrombosis. Venography was unfortunately not done. The varices were operated with multiple ligatures and she had no discomfort from the procedure.

This case was presented as an example of true abdominal wall varices, as distinguished from the dilated veins seen at portal hypertension and following iliac thromboses. It does, however, seem more probable that the etiologic agent of the dilated veins in the present case, as well as in that previously described, was an iliac thrombosis, even although there later has occurred a recanalization or, that also other anastomoses were developed, this being the reason for the operation not having more serious consequences. FROELICH (1934) states that there in 1 per cent of the patients with leg varices also are found abdominal wall varices. This figure is questioned by GOOEL (1944) who has examined 500 varices patients for abdominal wall varices without finding a single case. (His case just described did not have varices of the leg.)

Post-operative thromboses in the ordinary sense of the term (thrombosis without direct lesion of the vessel wall) are not expected taken into consideration in patients under 20 years of age. According to a personal communication by Dr. G. PETTERSSON, Surgeon-in-chief of the Gothenburg Children's Hospital, there have during his service as Chief (the last 4 years) not been seen any post-operative thromboses nor have there at all been seen thromboses except in marantic patients, or in direct association with a focus of infection. In large series of post-operative thromboses (PRIESTLEY and BARKER, RANZI and HUBER, SARAFOFF) there have been similar declarations. RANZI and HUBER say, in establishing that all of their thrombosis patients under 20 years of age have suffered from severe septic conditions: "In der Jugend bei gesundem Herz und unveränderter Gefässwand ist scheinbar nur die Entzündung imstande Thrombosen zu erzeugen." The patient with abdominal wall varices was only 14 years old at the time of the operation. He underwent an appendectomy with absence of infectious complications in the post-operative course and had nevertheless an iliac thrombosis. If this had been right-sided, one would probably have considered it to be caused by infectious or traumatic injury to the vessel, but now, as it was left-sided, it should probably in spite of the youth of the patient be termed a common post-operative thrombosis, with a probable origin in the pelvic veins.



Fig. 1.



Fig. 2.

OLSSON: Abdominal Wall Varices.



Fig. 3.



Fig. 4.

There are good possibilities for an anastomosis at an obliteration of the external iliac vein, with retention of saphena magna and the other superficial veins of the thigh. The superficial veins of the thigh merge into those of the torso like a coarsely meshed net in which certain large vessels may be distinguished, the external pudendal vein, the superficial epigastric vein on the anterior and the femoro-popliteal vein on the posterior side. The external pudendal vein is connected with the correspondent vessel on the opposite side. The epigastric veins have connections not only with the epigastric veins of the opposite side but also with the portal system at the umbilicus, with the internal mammary vein at the costal arch and, via the thoraco-epigastric vein, with the axillary vein. The femoro-popliteal vein empties into the inferior gluteal vein, a branch of the hypogastric vein, and may form an anastomosis between this and vena saphena parva. It is apparent that these collaterals after a short period of adaptation are capable of fairly well assuming the function of the iliac vein with regard to the leg, even though one can not count on such a speedy recovery and slight secondary symptoms as in the present case. The obliteration in this case involved a young individual still in the process of growth.

There was of course no question of operating this patient, so we had to rest content with explaining the cause of the varices, so that he at eventual future abdominal operations can ward off damage to the venous drainage of the left leg. It can not be considered advisable to perform multiple ligatures of the varicose vein at the site of the anastomosis with other vessels, as done by GOOEL in a similar case, as the venography so clearly indicates the course taken by the main volume of the blood. McLAUGHLIN and FROELICH advise the injection of common abdominal varices with the routine varices preparations.

### Summary.

The author reports a case of abdominal wall varices in a 28-year-old male, which debuted in connection with a left-sided thrombosis of the leg after an appendectomy at the age of 14. The clinical investigation showed that the flow in the abdominal wall varices was from the left to the right groin and that there was patency of the deep veins of the legs. At venography there was revealed the sudden termination of a large venous branch in the left groin,

the obliterated left iliac vein. The varices in the abdominal wall, some small veins in the pubic region, and the left iliac vein were seen to be contrast-filled. The patient had very little discomfort from his varices and no treatment was undertaken. The author has in the literature found a similar case, in which, however, venography had not been performed. The rare incidence of post-operative thromboses in the two first decades of life is pointed out by the author, and the good possibilities of anastomosis in cases of iliac thrombosis are described.

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## **"True Abacterial Pyuria".**

By  
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In 1913, at the Medical Congress in London, the Danish surgeon ROVSING declared that all cases of abacterial pyuria of renal type must, with certainty, be considered as tuberculosis and that nephrectomy should be carried out even if the bacteriological examination regarding tuberculosis were negative. At the present time this statement cannot be accepted without reservations. It has namely been pointed out and clearly established in a number of works that there are single or double-sided inflammatory changes in the kidneys and ureters with abacterial pyuria, and at the same time cystitis of a malignant type, without one being able to show the bacilli either with direct microscopic examination of the urine or with culture tests and animal inoculation. It has, however, been able to be established by means of clinical bacteriological and pathological anatomical investigations that tbc-bacilli are not the cause of the changes.

A not inconsiderable number of works has been published during the last two decades on abacterial (aseptic, amicrobic, sterile) pyuria without tbc. FALTIN, in 1909, seems to have been the first to describe this illness, yet without making any further attempts to determine its etiology or treatment. Since then a number of authors, not least from Scandinavia, have published works with a more detailed study of the illness (RUNEBERG, SÖDERLUND, TROELL, SCHAFFHAUSER, W. PETERS, BRIGGS, COOK, MOORE, UEBELHÖR, D. PETERS, WILDBOLZ, DONOVAN, HOUTAPPEL, etc.). In larger series than Runeberg's, Schaffhauser's and Th. Moore's are found detailed bacteriological and

histological studies. Smaller series and casuistic reports have contributed to make the illness better known, and shown that it is not so rare as one was inclined to believe at the beginning.

H. WILDBOLZ, in 1933, was probably the first to report on the specific treatment of this illness, when he pointed out at the French Urological Congress held in that year the immediate and excellent effect of arsenic compounds. After 1933 a number of authors gave reports on the thoroughly good results obtained by this treatment (BRIGGS, D. PETERS TH. MOORE, COOK, HOUTAPPEL, etc.).

One finds it stressed throughout that one only has the right to give the diagnosis abacterial pyuria if one can, by thorough investigation, exclude tbc. In the majority of cases this would seem to be possible, given the present clinical and bacteriological methods of investigation, and above all the roentgen rays. An equivalent sign between one-sided renal pyuria and tuberculosis has, for the majority of surgeons, undoubtedly signified and still does so, nephrectomy. This equivalent sign is responsible for the fact that the kidney that has been extirpated through the diagnosis tuberculosis has, in a certain number of cases, when investigated histologically, not shown itself to be the seat of tbc-like changes. If, in addition, an abacterial pyuria can give roentgenological changes at urography, insignificant indeed, of such an appearance that they cannot without difficulty be differentiated from a papilla destruction of a tuberculous nature, then the demand for a positive bacilli find, either directly under the microscope, or with guinea-pig inoculation, ought to be fulfilled before one resorts to nephrectomy. As the author recently observed two cases with presumably real abacterial pyuria with urographic changes, which could be interpreted as tuberculosis, it may be justified to give a report.

Nearly all cases described have a fairly uniform anamnesis. A number, the majority being anamnesticly varied cases, are considered by the majority of authors, who have busied themselves with relevant problems, to be of another genesis and probably to fall outside the larger group, which, in several places in the literature are linked to SÖDERLUND's name. This difference is especially upheld by WILDBOLDZ and SCHAFFHAUSER. The former holds that one must differentiate between, on one hand, the abacterial pyuria, which is a terminal stage of an urinal infection, primarily caused by coli or cocci, and, on the other

hand, a primary abacterial pyuria (= SÖDERLUND cases). The later sterile pyurian stage of the first group should according to TH. MOORE be considered as an analogy of the form of cholecystitis, where after a time a sterile gall-bladder content is obtained (GRAY 1936). SCHAFFHAUSER for his part holds that in several cases described in the literature as abacterial pyuria it is a question of apparently abacterial stages of acute or chronically infectious diseases of the kidney and renal pelvis (pyelitis, pyelonephritis, renal carbuncles, pyonephrosis), where, owing to unsatisfactory culture, the causal bacteria have not been successfully brought out. The etiology of these complaints is, according to the same author, not uniform. It is probably mostly a question of staphylococci, more rarely of strepto- and gonococci, or coli. SCHAFFHAUSER maintains that the similarity in the clinic, the anamnesis, and the course between his cases and those of SÖDERLUND is so pronounced, that one is justified in maintaining the probability of a special disease picture.

Some authors have only seen the illness in men, others only in women. The overwhelming majority of cases, however, seem to have been described in men. Where both men and women are concerned the greater number of cases were observed during the 20—50 years age group. In D. PETER's opinion the reason for this particular age group depends on the increased physiological and traumatic lesions to which the urogenital apparatus is exposed during the age of fertility.

When discussing the etiology one has mainly to deal with hypotheses. It is pointed out from various quarters that stones in the kidneys or ureters as well as chemical irritants for the kidneys, juxta-vesical inflammatory processes, cancer in the bladder and prostatitis, can give an abacterial pyuria. It may, therefore, be more correct to exclude these forms of abacterial pyuria and in conformity with T. MOORE use the narrower term "true abacterial pyuria". In RUNEBERG's material 30 cases are found in which could be demonstrated infectious processes in the kidneys of the pyelonephritis type appearing lymphogenously with interstitial lesions. In a number of these cases RUNEBERG found staphylococci at the histological investigation. RUNEBERG also holds that the constitutional anomalies (lobated kidney, renal cyst, aberrant renal vessels, outflow obstructions, etc.), often revealed in these cases, give a biologically inferior kidney predisposed to illness. RUNEBERG was, however, not successful



in isolating any bacilli forms when carrying out bacterial investigations of the urine. BRIGGS, among others, has adopted RÜNEBERG's assumption concerning the genesis of staphylococci. In 1937, SCHAUFFHAUSER contended that in certain cases of abacterial pyuria he could isolate streptococci, which only grew on special plates (Rosenow bouillon). He injected these bacterial cultures into the renal pelvis of dogs and in 50 % of cases obtained micro- and macroscopic changes of pyelitic type. These investigation results have, however, not been verified. COOK as well as SÖDERLUND and PETERS mention the possibility that toxins from the inflammatory foci might give an abacterial pyuria through renal influence, and the former, by reason of his opinion, adds to the treatment with arsenic compounds a purging of possible inflammatory foci. Otherwise he holds that a recurrence of the disease will be seen. The majority of the authors using the method of exclusion have finally adopted the theory that the cause of the disease must be a virus. The same authors consider that they are justified in this opinion by the fact that the pathological anatomical changes are of such a superficial character. Against the virus hypothesis it may be argued that the disease seems specially sensitive to arsenic compounds, at the same time as it is not influenced by sulfonamide preparations. Arsenic compounds were already in 1917 incorporated in the therapeutical armoury within urology, especially for use against staphylococci and certain forms of streptococci, and were shown to have a very good effect on these.

Three relatively hypothetical views can be crystallized from the etiological discussion. The abacterial pyuria might be caused by:

1) toxins from an inflamed focus located anywhere in the body (SÖDERLUND, PETERS, COOK, HOUTAPPEL);

2) cocci. RÜNEBERG's histological investigations point most closely to staphylococci. SCHAUFFHAUSER: in certain cases of the disease streptococci can be shown;

3) unknown cause, possibly virus. WILDBOLZ, HAMM, etc. These authors in general do not deny the above possibilities, but hold that not all cases of abacterial pyuria can be explained, but that it must be established that we ignore the cause in a number of cases (MCGINN).

A close study of the pathological, anatomical changes in the kidney and ureters has been carried out in various quarters in

the cases where an one-sided abacterial renal pyuria or one-sided urographic changes have led to the diagnosis tbc. ren. and nephrectomy. There is complete unanimity that the histological lesions found in real abacterial pyuria are very superficial and are freely classified as pyelitis and ureteritis follicularis. Histologically these changes appear like changes similar to lymph corpuscles and localized in the mucosa with relatively insignificant leucocytic infiltration. These lesions do not penetrate lower than into the sub-mucosa, for which reason a fairly swift restitutio ad integrum takes place after adequate treatment. The cases, of which there is a description (RUNEBERG, PETERS, TROELL), in which there also occur histological changes in the renal parenchyma of the focal glomerulonephritis or pyelonephritis type, probably do not belong to the group "true abacterial pyuria" but should be considered as the after-effect of chronic infectious pyelonephritis. RUNEBERG is himself of this opinion, which is also vigorously upheld by SCHAFFHAUSER. This supposition is also in harmony with the clinical observation that the RUNEBERG group often has an insignificant reduction of the renal function, whereas the SÖDERLUND cases almost always show an untouched function. The exceptionally demonstrable functional reduction in these latter cases are considered as a toxic renal influence (SÖDERLUND, SCHAFFHAUSER).

The disease clinically manifests itself mostly as a cystitis with frequent and repeated urination, smarting pains and aches in the urethra, pains in the bladder region and sometimes haematuria also occurs. The onset of the disease may be acute with urgent difficulties of the above-mentioned kind, but never with high fever nor disturbance of the general health. Also, in the further course of the disease the patients are mostly unaffected, with a good general health condition and without any increase in pulse or temperature. Epididymitis does not appear to be one of the complications described.

The duration of the disease can vary in the highest degree and a number of cases can certainly disappear spontaneously (author's case 2) or with constant treatment of the inflamed condition in the urinary apparatus. On analysing the urine a strong pyuria is found, but no bacterias. Culture is negative. Tbc-bacilli cannot be shown from direct tests nor from guinea-pig tests. External genitalia, prostate and ves. sem. are without remark. The female internal genitalia are not changed. The renal

function is most often untouched. Cystoscopy gives the picture of general, often haemorrhagic cystitis, with pronounced oedema and with fibrin formations. The picture differs considerably from the tbc one, with the latter's specific lesions alternating with parts of normal bladder mucous membrane, if secondary infection has not arisen.

On catheterization there were obtained in the catheterized urine leucocytes either from one or from both kidneys. In almost all cases in the literature, in which details are given of the bladder capacity, this is reduced and in many cases this reduction is so excessive that if cystoscopy can be carried out at all, it must be done with a lumbar anaesthetic.

Concerning the changes, which could be received with urography, mention will be made later on after a few cases have been reported.

*Case 1.* Journal no. 1776/47. 49-year-old man, previously healthy, fell ill directly after the New Year 1946—1947 with increased urination, pains and aches in the urethra in connection with urination. Urine turbid, and in a few cases mingled with blood. Venereal disease denied. Admitted to a hospital at the end of March 1947. On arrival, rather disturbed on account of his pronounced urinating difficulties. Non-feverish. N. P. N. 38 mg %. SR 39. Sed.: masses of red and white blood corpuscles. *Urography*: bad filling of left renal pelvis. *Cystoscopy*: bladder capacity 100 cc. Very turbid content in the bladder and on account of pains the cystoscopy is broken off. No tbc. bacilli in the urine. An iritis in both eyes was confirmed and he was consequently referred to the eye clinic of Lund's hospital. *Diagnosis*: tbc. ren.? On April the 28th, 1947, he was admitted to the surgical clinic, Lund. His condition grew worse. Urgent urinations day and night. Thick turbid urine. Aching in the urethra, and pains over the bladder without emission. Appetite bad, grown thin. Sleep rendered impossible by urgent urination. On arrival, relatively good general condition. Non-feverish. Bilateral iritis. External genitals without remark. Prostate normal size, of normal consistency, no tenderness. N. P. N. 33 mg %. Investigation of sediment (9 investigations): masses of leucocytes. No bacteria. Mantoux 1 : 100 strongly positive. SR 17. Guinea-pig test neg. *Urography* 2/5: a caudally directed calyx on the right side shows blurred contours. Bad contrast saturation on left side. Bladder small. (NORMAN.) 7/5: Left side without remark. On the right side normal calyces with the exception of a downwards-medial directed calyx, where the contrast collects itself into a »lake», scarcely the size of a grain of pepper, a little distance away from the calyx-contour. An incipient papilla destruction cannot be excluded. The bladder small. (HELLMER.) — 9/5 *cystoscopy* (JÖNSSON): Held < 200 cc. with stretching in lumbar anaesthetic. Extremely inflamed slightly bleeding mucous membrane.

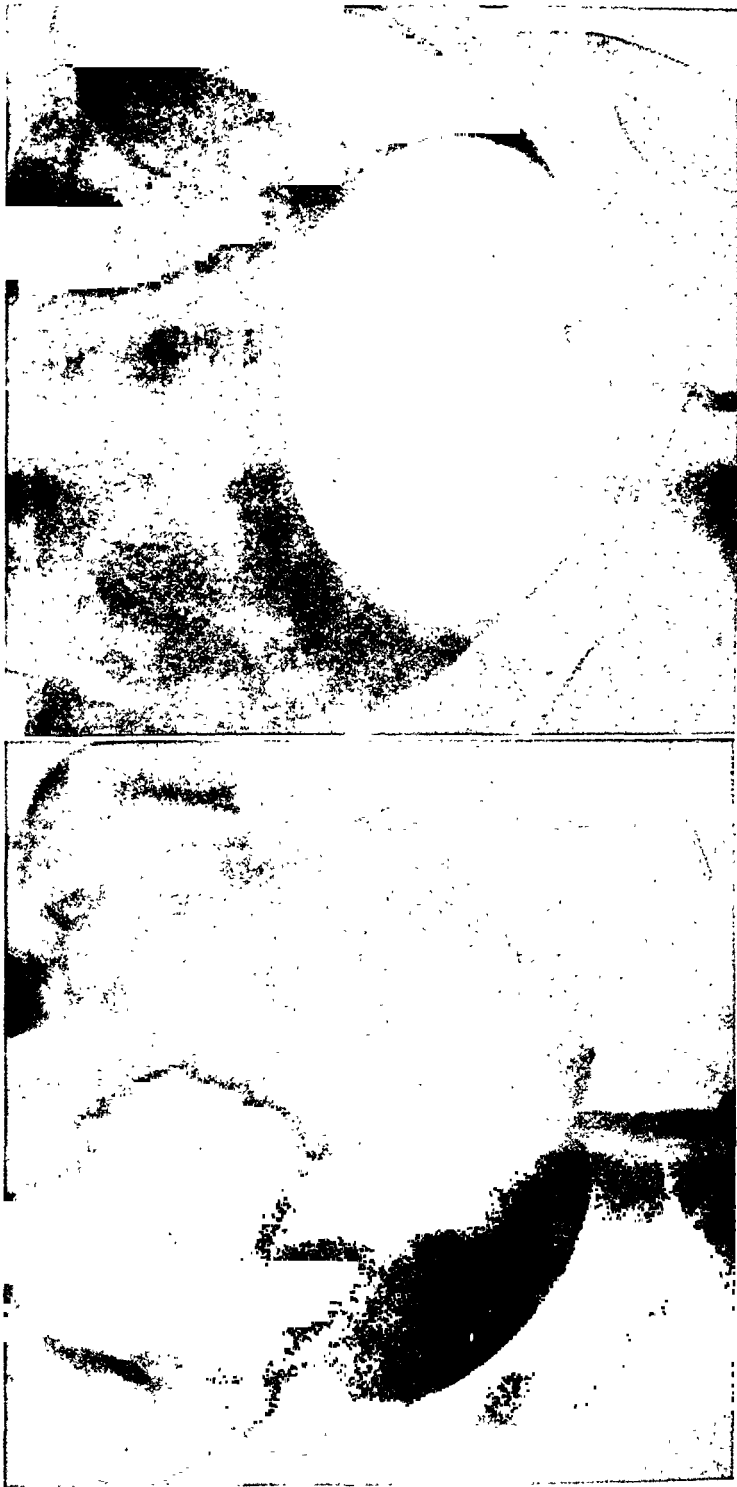


Case I urography 12. 6. 1947.

Case II urography 5. 11. 1947.

Fig. 1.

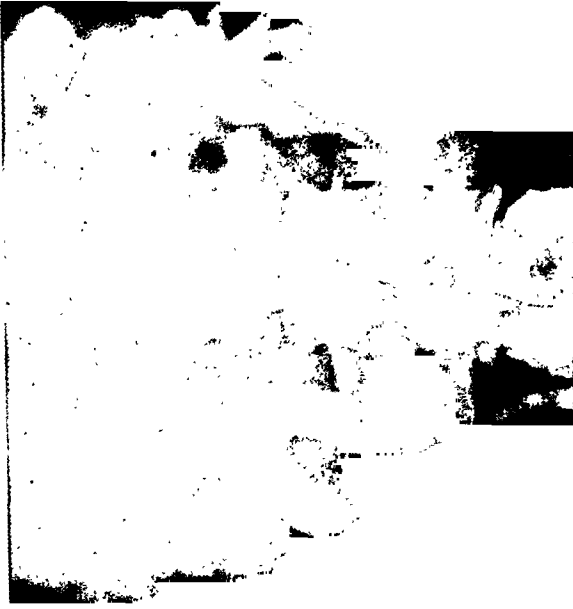
JÖNSSON: "True Abacterial Pyuria".



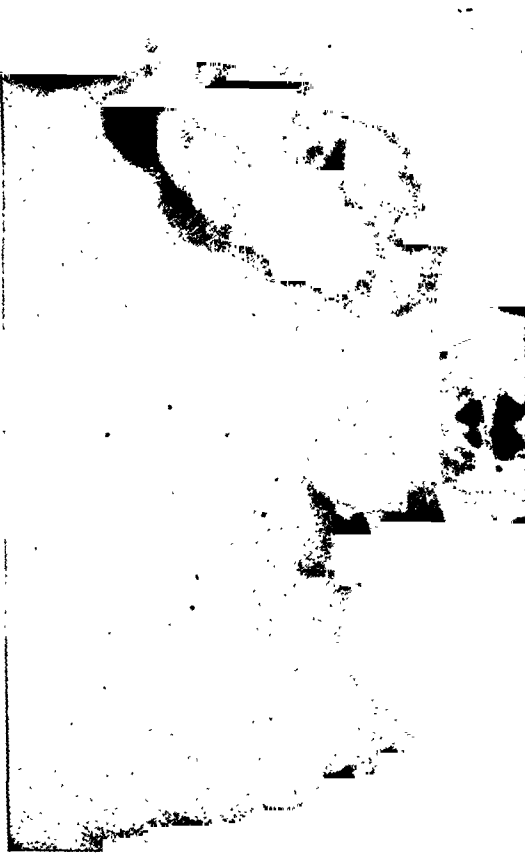
Case I urography 12. 6. 1947.

Case I urography 5. 11. 1947.

Fig. 2.



Case II urography 29. 7. 1947.



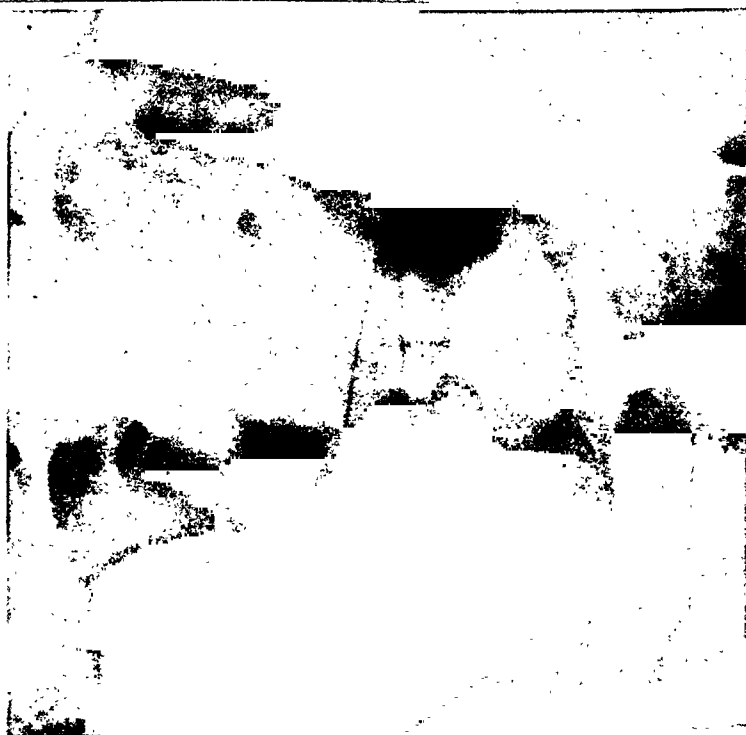
Case II urography 27. 1. 1941.

Fig. 3.

JÖNSSON: "True Abacterial Pyuria".



Case II urography 29. 7. 1947.



Case II urography 27. 1. 1941.

Plentiful deposit. Difficult lavage. Culture: no growth. — Discharged on the 10/5 pending guinea-pig tests. He is strongly suspected of the ren. — Treated again 30/5—25/7 1947 by reason of difficulties having further increased. Pains now so intense, that the patient could not manage without morphine. On arrival the patient's condition was fairly disturbed. His status otherwise unchanged. Iritis also unchanged. Fresh *urography* on the 12/6: the rightside calyx change appears as before. On the left side a delayed discharge and dilatation of the pelvis and ureter have arisen. The bladder small as before. (Fig. 1 and 2.) — After repeated investigations the sediment was found to contain masses of white blood corpuscles but no bacteria. Culture was carried out on three occasions and showed no growth except on the last occasion when enterococci were obtained. — The condition was one of exceptional difficulty for the patient. A penicillin- and sulphadital cure was introduced (20,000 E  $\times$  8 and 2 tabl.  $\times$  4). No improvement could be noted; if anything, the patient's condition deteriorated. The possibility was then discussed of carrying out a ureter transplantation according to COFFEY's method, and in spite of negative guinea-pig tests there was talk of a nephrectomy on the right side. Neosalvarsan was given in five injections from 3/7—13/7 in doses of 0.15 gr. After this treatment the patient was as good as relieved of pain. The effect was striking. The urinating frequency sank to once every two or three hours. No pains and no ache. The subjective improvement was also reflected in the objective investigation results. — *Cystoscopy* 11/7 (JÖNSSON): The bladder holds 70 cc. Less inflammation of the mucous membrane. Both ureter orifices now visible. — 21/7 *urography*: some bilateral dilatation. No signs of destructive process. Investigation of earlier urograms shows that the change suspected of being a destructive process is probably represented by an unusual grouping and form of calyces. (OLLE OLSSON) — 21/7 *cystoscopy*: content 100 cc. Mucous membrane still inflamed. Fibrin coating backwards. The right ureter orifice without remark. The left cannot be observed. — On the 25/7 the patient was discharged in good condition and with an almost normal urination frequency. No subjective trouble. The iritis rapidly improved during the last week before discharge. — Was taken in again in November 1947. Had then been in full employment. No urination troubles whatsoever. The urination frequency was 5—6 times a day, and 1—3 times a night. Urine clear all the time. The patient's general condition appeared good. The prostate and external genitalia as before. N. P. N. 35 mg %. Three sediment investigations showed that the urine contained single white blood corpuscles. *Urography* 5/11: simultaneous and at the normal time discharge on both sides. Normal pelvis morphology. Bladder normal size. (OLLE OLSSON.) (Fig. 1 and 2.) — *Cystoscopy* in local anaesthetic: quite pale and normal bladder mucous membrane. Content 150 ml without stretching. Ureter orifices without remark.

Case 2. Journal no. 428/41. 27-year-old man, who, in February 1940, began to have urinary trouble. The frequency increased to one



every half hour. The urine was very turbid. Troubled by dull grinding pains in the perineum. Venereal disease was denied. He was admitted to the clinic on the 24th Jan. 1941. The patient seemed to be in good condition. Non-feverish. External genitalia without remark. The prostate normal size and of normal consistency. Slight tenderness over the left vesicul. seminal. N. P. N. normal. Repeated sediment investigations showed masses of white blood corpuscles and up to ten or so red ones, but no bacteria. *Urography* 27/1 showed retarded discharge on both sides calyces and ureters dilated. The bladder only plum-sized. (Fig. 3 and 4.) The changes were interpreted in the first place as a bilateral renal tuberculosis. Guinea-pig tests were however negative. After having received a streptomine cure the patient's condition showed practically no improvement. No change in the sediment could be observed. Discharged with a tbc. diagnosis. His condition, however, was such that he could begin work again, which he then continued to do. He had pains periodically in the back and increased urination. Was admitted again in March 1946 for control of his condition. External genitals showed no change. N. P. N. normal. *Urography* 14/3-46 showed same status as in 1941, although the bladder was considerably larger. Sediment investigations showed masses of white blood corpuscles. Culture gave no growth. Guinea-pig tests from bladder and ureter urine were negative. *Cystoscopy* showed an intense inflammation of mucous membrane and plentiful fibrin clots. Content 100 ml. For further control the patient was admitted afresh on the 28/10 1947. He had been in work, which had not taxed his strength. Urine was still turbid. Urination frequency by day 4—5 times, and by night 2—3 times. Insignificant smarting pains. N. P. N. normal. *Urography* 29/7: Size, place and form of the kidneys show nothing pathological. No calcifications. Simultaneous, and at normal time, discharges on both sides. Since the 1946 investigation the enlargement of the left pelvis and ureter had further receded. The right pelvis still shows an enlargement like the ureter. The bladder has further increased in volume. (OLLE OLSSON.) (Fig. 3 and 4.) *Cystoscopy*: content 200 ml without stretching. The mucous membrane in the trigonum is rather edematous and coated with fibrin fur. Ureter orifices somewhat edematous. (JÖNSSON.) Four sediment investigations showed plentiful white blood corpuscles. Three culture tests in urine: enterococci. On the 30/10 neosalvarsan treatment was begun in doses of 0.30 gm in three injections in three-day intervals. On visiting the polyclinic on the 18/11 the patient stated that he was now entirely free of trouble. No urination at night and normal frequency by day.

As is seen there appear in the author's cases changes of such a character urographically that tbc. can be suspected. When one, moreover, has an abacterial pyuria, the diagnosis tbc. is, of course, the most obvious. But the repeated tbc-investigations insist on giving a negative result. But here, as always, one must make a point of including the roentgen investigation as part and

parcel of the urological investigation, which cannot replace the other investigations.

Urography as an investigation method is relatively young, for which reason a number of the cases described in the literature of abacterial pyuria have not been subjected to this especially fruitful and valuable investigation. The changes, if any such are to be found, which can be registered at an intravenous urogram, are principally a dilatation of the pelvis and ureters (MOORE, COOK, DONOVAN, MCGINN, HAMM). The differential diagnostical difficulties with urography between tbc. and true abacterial pyuria have been pointed out by LJUNGGREN and OLLE OLSSON as well as UEBELHÖR.

LJUNGGREN points out that one, with cases of sterile pyuria, which must always of course be first and foremost suspected as tbc., often begins the urological investigation with urography and if one gets a positive answer for tbc., the further search for tbc-bacilli is gladly dispensed with. Here one must, like LJUNGGREN, issue a warning. The diagnosis tbc. is only 100 % safe when tbc-bacilli have been demonstrated. A saying of SINZ is worthy of quotation. The latter holds that it is of great value that the diagnosis of a renal tbc. in certain cases can be proved by X-ray; in this manner time is gained and an operation can be carried out before the results of the animal tests are clear. This opinion of the importance of gaining time in cases with tbc., a chronically drawn out illness, is completely out of harmony with the present day opinion about the most suitable time for operations in such cases. Moreover, with this opinion, one should not be able to shut one's eyes to a certain number of cases, in which the operation will be carried out on a wrong diagnosis. Case no. 1, described above, would possibly have fulfilled SINZ' claims for a nephrectomy; but for the surgeon it would have meant a wrong diagnosis and for the patient an irrelevant interference, by which he would have been deprived of an organ, which later with adequate treatment would have shown itself to be normal. In 1936 UEBELHÖR also takes SINZ to task, and points out that at the operation of an early tbc., often impossible on the free kidney, one can read whether the tbc. lesions are there or not. UEBELHÖR reports a case, in which urography showed changes in the form of a blurred calyx on one kidney. The patient had a sterile pyuria, which clinically agreed with tbc., and underwent an operation. The histological examination, however, showed no tbc-lesions but a pyelitis follicularis.

LJUNGGREN and OLLE OLSSON discuss papilla necroses of a different kind in their works on the urography of tbc. and on its importance for the differential diagnosis for tbc. Among other things they mention papilla necroses in diabetes, pelvis tumours, pyelogenic cysts and pyelitis follicularis. This latter form can, as in UEBELHÖR's case, by its changes in the mucous and sub-mucous give urographic changes in the shape of blurred calyx contours or in the shape of dilatation of the peripheral calyx part, brought on by an obstructed outflow owing to the swollen mucous membrane centrally opposed to the pelvis.

These urographic lesions in abacterial pyuria could be highly similar to those obtained in a tbc. in its earlier stage. Both OLLE OLSSON as well as LJUNGGREN issue a warning, therefore, against making a diagnosis of tbc. only from an urogram, without at the same time having made a strict comparison between the roentgenological and clinical findings.

In the cases observed, reported on and treated, at the surgical clinic in Lund, are found urographical changes, which could be taken for an initial destructive process of tbc-character. The comparison of the clinical symptoms and the investigation results brought it about that, pending the guinea-pig tests, the advance diagnosis of tbc was passed. The fact that nephrectomy was not carried out in case no. 1, where the changes were of a one-sided type, depended on a wish to await several microscopic tests and the reactions to the guinea-pig test. Nor was the cystoscopic picture typical in appearance for tbc. If one had been of opinion, in accordance with SINZ, that one ought to gain time by a nephrectomy, this would have resulted in the removal of a "fresh" kidney. The diagnosis true abacterial pyuria was not passed before two guinea-pig tests had proved negative, and the striking result with neosalvarsan had been observed. The fact that the diagnosis tbc could be entirely relinquished can be partially attributed to having obtained a fully normal urogram after neosalvarsan treatment. This latter circumstance is of especial interest, since only a few cases of true abacterial pyuria have been described in current literature, in which the urographic changes have been followed both before and after treatment, and shown regression (CHARLES TAHARA and associates, HAMM and MCGINN). Just as in these two cases that have been described, so all cases, reported as belonging to this disease group, do not seem to show any weakening of the renal function. Throughout the patients are not dis-

tressed and are without fever and pulse increase, but in the author's case no. 1 the patient's urinary trouble was urgent and entirely disabled him. These discomforts forcibly remind one of the bladder troubles, seen in advanced tuberculosis of the bladder. Here it was even a question of an ureter transplantation, when the patient had defied the usual treatment and himself signified that he could no longer hold out against his condition.

The second case has shown, after having first fallen ill seven years previously, a remarkable regression of both objective findings as well as subjective troubles. One might with justice be permitted to consider the case as one of spontaneous healing. The attempt made, as a result of the successful outcome of the first case, to try and influence the illness so late as now, has, nevertheless, entirely freed him from the subjective troubles, although he still has a pyuria. The enterococci, which can in both cases be shown in the advanced course of the disease, could probably be explained as introduced into the bladder when draining and performing cystoscopy.

Both cases appear to the author to be in perfect accord with the majority of the examples of "true abacterial pyuria" described as SÖDERLUND cases. The good result of the neosalvarsan treatment is striking. A regression of the urographic changes and of pyuria can also be shown in the first case after neosalvarsan treatment.

### Summary.

After a short survey of the literature on abacterial pyurias with mention of different hypotheses for their genesis, pathological-anatomical picture and clinic, two cases are reported, which probably belong to the group "*true abacterial pyuria*". Treatment was carried out with neosalvarsan in accordance with the directives given by WILDBOLZ. A striking effect can be shown and the regression of the urographical changes pointed out. The differential diagnostical difficulties in the both from a roentgen and clinical view-point are emphasized. The author maintains that an equal sign cannot generally be placed between abacterial pyuria and renal tuberculosis, not even if the changes shown on the urogram are of the type. The decisive factor for the final tuberculous diagnosis must either be the showing of tuberculous bacilli or a critically drawn-up comparison of the urographic findings and the clinical ones.

Otherwise a certain number of patients with abacterial pyuria, not due to tbc. must with all certainty be treated as a renal tbc. and thereby be exposed to such a crippling intervention as a nephrectomy. If the correct diagnosis, "*true abacterial pyuria*", is not given, so that adequate treatment can be undertaken, the disease will most often acquire a long-drawn-out course with greatly reduced bladder capacity, and therewith the patient generally falls into the same miserable condition as patients with tuberculosis of the bladder. With correct treatment the prognosis seems to be excellent.

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## Recent Advance in Krukenberg's Operation.

By

K. E. KALLIO.

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KRUKENBERG's ingenious idea to transform a forearm stump into a forceps-like new hand, a gripping organ with sensation, to be used just as it is, without a prosthesis, was introduced as early as 1917, but so far little attention has been paid to it.

### Survey of the Literature.

*Germany.* — At the Hamburg Medical Society, in 1918, KÜMMEL gave an account of the operation, and DENK published one case in the same year. The next year KÜMMEL had seven cases operated on, of which FLOCKEMAN demonstrated three particularly successful cases in Hamburg and two at the meeting of surgeons in Berlin in 1920, where BORCHARDT, too, demonstrated two cases of his own. SAUERBRUCH, who a few years earlier had published his own well-known kineplasty, said, at this meeting, about the Kr operation: "Für doppelamputierte und blinde ist die KRUKENBERG-operation das Verfahren der Wahl. Hier leistet sie mehr als irgend eine andere Methode." In the same year SCHEEL recommended the procedure for all bilateral cases, yet emphasizing simultaneously the value of a prosthesis. In 1922 FRAENKEL published a case where the claw had a grasping power of 2 kg. Four years later LOTSCH discussed the question in an article published in *Die Chirurgie*. KRUKENBERG himself defended his operation in 1928. The following year SCHNEIDER published two and REY three cases. In 1930 PORZELT, reporting on three cases of his own, suggested that the ends of the bones be not grooved. He considered thirty degrees as the optimal opening

angle for the claw and recommended that the branches be 14 cm long. He was also of the opinion that this plastic operation should not be made on blind persons or on those over sixty years of age. In the same year SCHLIEPE, at the German Orthopedic Congress, presented the results of fifteen operations which he had made himself in the years 1918—30. Two of these cases were bilateral. He had arrived at the conclusion that the operation is always indicated unless the patient is blind, providing the stump is at least 12 cm long. The length of the branches ranged between nine and fourteen cm in his cases. SCHLIEPE had removed the flexores digitorum profundi and the muscles of the thumb. In his cases the closing of the claw was not a pure hinge-like movement of the radio-ulnar joint but a combined rotating movement. He emphasized, further, that the new hand must be capable of opening and closing when the forearm is stretched out as well as when this is bent and that the opening angle must be at least thirty degrees. In cases of bilateral amputation he recommended that a movable KRUKENBERG prosthesis be applied to one arm, while for those with one hand left no prosthesis was needed. SCHLIEPE was highly satisfied with the results obtained because the patients were able to employ the claw, which made self-supporting even the bilateral amputees. In 1931 KRUKENBERG published his observations from a period of fourteen years. The shortest stump on which kineplasty is advisable, he thought, must not be less than 12 cm. The operation should not be performed on a person who has one hand left unless he asks for it or is insured. In the same year he issued a warning against the use of a prosthesis, which destroys the function of the claw. Von HABERER reported on five successful cases, wondering why it is that patients are not easily persuaded to undergo this operation. NISSEN, in 1933, gave an account of the technique of KRUKENBERG's operation. During World War II KREUZ vigorously advocated this procedure.

*Russia.* — In 1923 ROSANOFF published two cases where the patients were able to eat and write by means of the new hands. HEIMANOVICH, who in 1928 published one case, preferred the procedure to the use of a prosthesis. The next year N. PRIOROV reported on two cases from the orthopedic institute of Moscow University, recommending removal of unnecessary muscles to enable the skin to cover the new fingers. GINSBURG, in 1930, had one case, in which the operation had been made on a one-handed patient with success. He felt that this valuable procedure had not

been sufficiently appreciated. In the Russian literature he had only found nine published cases. The next year this number was increased by one one-handed case operated on by RUDNICKIJ. N. PRIOROV appears to have the largest experience on this question. In 1935 he published his observations on seventeen cases, in which the results were particularly good on persons who had lost their both hands. In the same year SILBERBERG reported on one successful bilateral case and in 1937 VOROBYEV two one-handed cases. He suggested that the bone be shortened in a long stump, to make the skin cover the new fingers. KALMANOWSKIJ published in 1939 the interesting investigation which he had carried out on the antebrachial circulation of blood by means of contrast medium and X-rays. This showed that the following muscles had to be retained at the operation to secure circulation of blood in the stump: the m. brachio-radialis, the extensores carpi radialis, the m. flexor et extensor carpi ulnaris, the mm. supinatores et pronator teres. If these are retained, the skin of the stump is sufficient to cover the branches of the new hand, as stated by KALMANOVSKIJ a year later. ALBRECHT recommended removal of the muscles down to the supinators and the pronator.

*Poland.* — Muscle-poor, thin branches were particularly recommended by LATKOWSKI, who, in 1926, stated that only four muscles had to be retained at the operation, namely the m. ext. carpi radialis and brachio-radialis as abductors and the m. flex. carpi radialis and m. flex. dig. sublimis as adductors. Two years later he had three such cases.

*Britain.* — THOMAS PURCE reported in 1939 on a successful KRUKENBERG operation performed on a negro whose left hand had been bitten off by a leopard. He said that in British surgical literature he had only come across one publication dealing with the subject, viz. that of B. T. SQUIRES from the year 1937. SQUIRES's two grateful patients were likewise coloured people, and he recommends the procedure particularly for the colonies, where no great attention is paid by the natives to the aesthetic side of the question.

*U. S. A.* — COLP and RANSOHOFF collaborated in a report on two cases (illustrated by photographs) from 1933. This was probably the first American publication on the subject, and the writers said that the procedure was little known in that country. RUDOLPH NISSEN and ERNST BERGMANN, two German surgeons who had settled in the U. S., made an attempt to advocate kineplastic



operations by publishing, in 1942, a book in which, among other things, they gave a description of the German Kr technique. The operation, however, did not arouse any great interest, and in his book published in 1946 ARTHUR STEINDLER thinks that the method is no longer used. In the same year MCKEEVER stated that kineplastic operations were of no value except to bilateral forearm amputees, and RANK and HENDERSON recommended for such cases SAUERBRUCH's kineplasty with a prosthesis. In his work entitled *Cineplasty* (1947) HENRY H. KESSLER, who has done much to introduce SAUERBRUCH's kineplasty into the U. S. after World War II, writes appreciatingly of the Kr operation and recommends it for blind people and for bilateral amputees.

In 1947—48 the present writer made a long tour in the U. S. He found that the method had not been accepted for general use, and this for the following reasons. First, because it was said that it was difficult to persuade people to undergo the operation (as has, at first, been the case in every country). Second, because the orthopedists did not think highly of a gripping movement which, according to reports published so far, was done by rotation.

In the *Spanish-speaking world* the method likewise seems to be very rare. In 1926 ANTONIO OLLER emphasized that the traumatic shock due to the operation is great even if the skin of the stump could be made to cover the branches. GARZIA had one case in 1939, and in the same year PEÑAFORT gave an account (with cinematographic demonstration) of the Argentine modification of the procedure, in which all muscles of the stump were removed with the exception of the supinators and the pronator.

*Hungary.* — SZENES (1920) carried out post-mortem studies on the procedure and BAKAY (1925) wrote in favour of it.

*France.* — In the literature of this country the present writer has failed to find any publication dealing with the Kr operation, and it is significant that in the new comprehensive French manual of surgical technique, to which S. OBERLIN has contributed a chapter on kineplasty, there is only a passing reference to the Kr operation, with a drawing representing a short division of a long stump, with arrows to indicate that the closing of the claw is a pure rotating movement. (Probably the drawing does not illustrate KRUKENBERG's but LAMBRET's operation.)

In *Scandinavia* there have been no publications on this subject. In *Finland*, the first Kr operation was performed in 1928 by KALIMA. The writer had an opportunity of assisting him at an-

other operation in the following year. About the same time the operation had also been performed by LANGENSKIÖLD, the writer's present principal, whose experience comprised several Kr cases by the outbreak of World War II.

The following table is a survey of all publications on the KRUKENBERG operation of which the writer is aware:

Country	Period	No. of Publications	No. of Cases
Germany .....	1917—42	15	45
Russia .....	1923—39	8	30
Poland .....	1926—28	2	3
Britain .....	1937—39	2	3
U. S. A. ....	1933—46	1	2
Spain .....	1926—39	2	1
Total .....	1917—46	30	84

This shows that surprisingly little has been written about the procedure and that practically taken it has only been used in Germany and Russia, particularly during World War II (KREUZ, PRIOROV). After having seen in Berlin claws "closing in pronation", M. PERKINS of Britain has strongly pleaded in favour of this operation at the 1946 international orthopedic congress, which on this occasion was met with general approval. This has made KRUKENBERG's idea a question of actual importance.

## Own Experience.

### I. Material.

This investigation deals only with cases treated personally by the writer. They are unselected and consecutive. The series consisted of altogether forty-five new hands. Three bilateral amputees underwent an operation on both stumps, the number of patients being thus forty-two. With the exception of four, they were all disabled servicemen. Except for one aged fifty years, the patients did not exceed thirty-five years of age. The youngest patient was eight years old. Thirty-nine patients were male and three female.

*Injury.* — It is not without interest to find that the majority of patients, twenty-seven in number, more or less owed the loss of their hand to carelessness. Twenty-two patients, for example, had kept some explosive thing in their hand and thus caused the

injury themselves. In seven cases a mine had exploded in the patient's hand, in eight a hand-grenade, in three a T. N. T. charge, in two a blast, in one a fuse, a trinite or dynamite charge. In one case a high tension electric current had caused the loss of the hand. Besides, a drunken man (Case 40) had got under a train and another (Case 19), the oldest patient in the material, had both his upper limbs frozen when he had to spend a whole night on the open platform of a sleeping car in extremely cold weather. In three cases the hand had been lost at a chaff-cutter and in two at a circular saw. In the other cases loss of the hand had taken place on the battlefield. Several patients had simultaneously received other injuries, particularly ocular lesions.

*Proposal of Operation.* — All the 186 patients with amputation of the forearm treated at the hospital were at first meeting shown a new hand, followed by a proposal of an operation. Those who had lost their both hands or had severe injuries readily accepted the proposal, as did those with severe eye lesions, while patients with unilateral amputation, who had one hand left intact, adopted, without exception a hesitating attitude. After having met at the hospital friends who had undergone the operation, approximately every fourth of them accepted the procedure to be performed on themselves.

*Time of Operation.* — More than a half of the operations were performed half a year or less after the amputation. In some cases, however, the interval was even more than two years. The writer thinks it advisable to perform the operation before the patient gets used to the condition following the amputation.

## II. Treatment and Care.

### *A. Operation.*

In *Krukenberg's original kineplastic operation* the forearm stump is cleft and formed into a kind of forceps the radial branch of which is made to move actively against the ulnar branch. At the operation, the m. brachio-radialis, the supinator muscles, and the m. pronator teres are left intact. The radial flexor and the radial extensors remain in the radial branch and the ulnar flexor and the extensor in the ulnar branch, while the m. flexor digitorum sublimis and the m. ext. digit. communis are divided equally between the two branches. The flexores digitorum profundi and the muscles of the thumb are removed before the membrana

interossea is split. The skin of the forearm is then cut with a U-shaped incision so that it is sufficient to cover the radial branch of the claw. KRUKENBERG himself aimed at the skin of the stump being sufficient to cover both branches. In case it is not, the ulnar branch has to be covered with a pedicle skin flap taken from the side of the abdomen. This pedicle skin flap was transplanted on the medial contact surface of the ulnar branch (as seen for instance in NISSEN-BERGMANN's book) and as far as is known the gripping movements of the KRUKENBERG hands were combined with pronation—supination.

*Modifications.* — Attempts have been made to simplify the Kr operation so as to make the skin of the forearm stump cover both branches. In order to achieve this, shortening of the bones in the stump (VOROBJEV) or removal of muscles (PRIOROV, KALMANOWSKIJ) has been suggested. ALBRECHT has even proposed the removal of all muscles except the pronators and supinators, and LATKOWSKI has only retained four muscles, viz. the radial flexor and extensor, the m. brachio-radialis, and the m. flexor digitorum sublimis. KREUZ, with whom the present writer had an opportunity of studying orthopedic surgery in injuries of the upper limbs in Berlin in 1942, said that it was difficult to persuade disabled soldiers to undergo a two-stage operation. For this reason, whenever possible, he used a one-stage operation in which the bones of the stump were shortened but no muscles removed unless this was absolutely necessary. This often resulted in a clumsy claw, and cosmetic surgery was often called for later. The procedure used by KREUZ, the writer feels, is quite appropriate when the stump is too long. Otherwise he cannot share the view of those who aim at one-stage operation because this often impairs the final result.

*The Writer's Technique.*<sup>1</sup> — In principle, the writer prefers operation in two stages because this allows an entirely free treatment of the muscles and the skin. Not a single muscle is removed. They are grouped so as to leave the tendons cicatrised at the end of the stump intact if possible.

For an operation performed in two stages the skin of the stump has been split in the following manner which the writer has learnt from LANGENSKIÖLD and which he prefers to any other

<sup>1</sup> I am taking this opportunity of thanking Dr. P. G. K. BENTZON of Aarhus, Denmark, who has kindly prepared a cinematographic film on my technique of operation.

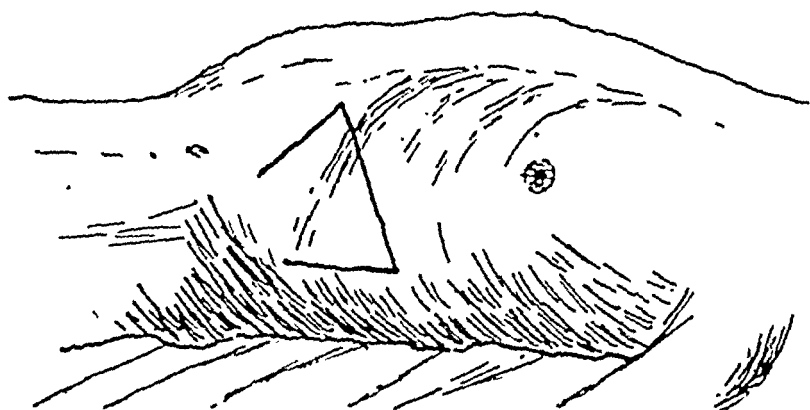


Fig. 1. Incision used by the writer.

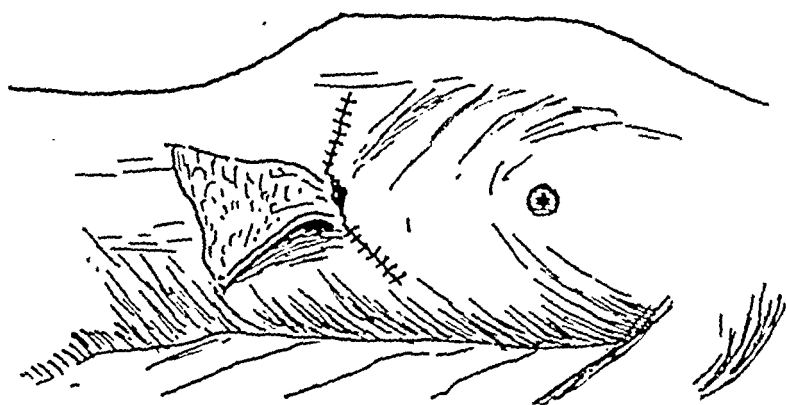


Fig. 2. The flap of skin turned downwards and the defect closed by suture.

skin incision known to him: A longitudinal incision is made on the dorsal aspect of the forearm along the ulnar side of the ulna. On the volar aspect the incision is made slightly radially from the midline. At the proximal end these incisions curve so as to resemble the figure of a fish-hook, the dorsal incision radially, the volar ulnarly. On the dorsal aspect the skin is then prepared slightly radially and on the volar aspect slightly ulnarly so as to form two flaps of skin. When the splitting of the stump is finished, the dorsal flap is turned round the radius and its edge is sutured to the radial edge of the volar incision. The volar flap of skin is now turned round the ulnar branch. This, however, is so small that it only covers the volar aspect of the ulnar branch. The skin defect on the outer side of the ulnar branch is covered with a pedicle skin graft from the side of the abdomen. The skin graft is not

used to cover the contact surface. For this important phase the author has developed a method of his own, which is as follows:

The flap of skin is made from the side of the abdomen so that its base, situated caudally, is somewhat narrower than the loose distal end. Thus, when the flap is free and turned upside down; it forms, together with the defect, a figure resembling an hour-glass. This method has two remarkable advantages, viz. 1) the



Fig. 3. The transplanted skin flap covers the dorsal aspect of the ulnar branch.

narrow-based defect on the abdomen can immediately be closed, starting from the sharp angles, the result being a V-shaped suture, and 2) the flap being caudally attached to the skin of the abdomen, its free portion is easily turned into the dorsal surface of the ulnar branch, to which it is sutured (Figs. 1, 2, and 3).

The author's operative method has the following important advantages: First, since it is not necessary to remove any muscles, the blood supply in the branches remains better and the claw has a more agreeable appearance. Second, the skin to cover the branches can be sutured without any tension and the scars placed outside the contact surfaces, so that a good sensation is obtained. Third, since the skin defect on the abdomen can be closed primarily, the patients are not afraid of the two-staged operation.

The writer, however, has not always followed the aforementioned procedure. He has twice performed a two-stage operation according to the original KRUKENBERG method, *i. e.*, by removing the flexores digitorum profundi and the muscles of the thumb (2 and 25). In five cases where there has seemed to be plenty of skin on the stump, he has ventured to perform the operation in one stage (5, 32, 34, 37, and 40), but in these cases it has been

necessary to remove the same muscles as in the two aforementioned cases. In one case (3) he sutured the tendons over grooves made on the ends of the bones, which resulted in osteitis and silk fistulae. In four cases with a short stump and plenty of skin a successful one-stage Kr operation was made without removal of muscles (Nos. 8, 33, 35, and 36). In such cases as these the procedure, of course, is indicated, but even here the evaluation of the case is difficult and the question of the skin may easily make the operation exciting.

### *B. Supplementary Operations.*

In two cases an ulnar exostosis which had developed at the base of the branches and interfered with its movements had to be removed. Therefore, if the closing movement remains imperfect, it is always advisable to make an X-ray examination. Only two patients, both of them female, asked for a subsequent cosmetic operation on account of the scars of the stump.

### *C. Exercises.*

In a new hand the abductors of the radius consist of the m. brachio-radialis, the extensor carpi radialis, and the radial part of the m. extensor digitorum communis, the adductors consisting of the m. flexor carpi radialis and the radial part of the flexores digitorum. In the ulnar branch, the abductors consist of the m. extensor carpi ulnaris in co-operation with the ulnar part of the m. extensor digitorum communis, and the adductors of the m. flexor carpi ulnaris and the ulnar part of the flexores digitorum. Considering the power of these muscles, the writer feels that, from the beginning, the exercises must aim at pure ab—adduction, which is the only way to make a forceps-like hand a real gripping organ. If a claw is moved by a mere pro—supination mechanism, it grasps objects with difficulty or they tend to twist in it in an awkward manner, which renders the outcome of the treatment doubtful.

The writer has personally supervised the exercises in his cases. They are begun immediately after the removal of the sutures. It has been considered of outmost importance that even at the beginning the patients are not allowed to make pronation—supination movements. In teaching the patients pure ab—adduction the writer has used the following method worked out by himself: the operator has grasped the radial branch of the claw tightly and

asked the patient to bend simultaneously both his elbows: experience has shown that by doing so the ulna is invariably adduced straight against the radius. The ulna is then fixed up and the patient is asked to try and straighten his elbow-joint. The patient is interested when he finds that his forceps-like hand starts to work immediately and begins to perform this exercise himself.



Fig. 4. Handles for knife, fork and spoon (case 9).

The training thus takes a right direction from the very beginning and gets a good start, which otherwise is often a desperate affair. Those who had lost their both hands were, of course, the quickest to learn. The exercises have to be carried on in any case for several months, seeing at the same time that the patient begins to use the new hand when taking his meals, or writing, etc.

#### *D. Orthopedic Care.*

In order to enable the patient to make good use of the new hand even during the period of training he is made to write with a pen furnished with a wedge-shaped handle of cork. His fork, knife, and spoon likewise have special handles. Patients with bilateral amputation have been given boots without laces and furnished with special loops for pulling them on. The clothes are



furnished with zip-fasteners and the waistcoat and coat with special buttons.

The patient is given a prosthesis only when the new hand is fully trained. At first, everyone wanted to have a kinetic Kr-prosthesis, but, with the exception of two cases, they soon gave it up, preferring the combined prosthesis used by us, in which the cosmetic hand could be detached from the wrist and replaced by a utility hook and a pair of tongs. It is an important observation that bilateral amputees never wore a prosthesis on both arms: they feel helpless if they do not leave their right new hand free.

### III. Follow-up.

Questionnaires were answered by all patients except three. In addition, the writer carried out personal examination of the new hands, as seen from the enclosed table recording the results of the follow-up. To illustrate the matter he also had a cinematographic film made.

*Period of Observation.* — In thirty-seven cases the follow-up period lasted at least one year after the operation, although in six of these cases the information was only based on correspondence. Thirteen cases could be followed up for three years or more.

#### *A. Condition of the New Hand.*

The lengths of the Kr stumps, the distances between the tips of the branches, and the opening angles are shown in the table. A fifteen cm long stump gave a good result. KRUKENBERG himself considered twelve cm as the minimum length for the forearm stump. The writer, however, has a case with a claw made from a stump that was ten cm long; it shows good ab—adduction and the patient uses it instinctively (the other hand is badly damaged). A claw made from a thirty-one cm long stump was too long and proved a failure. To judge from the writer's material, the optimal length for the stump is two-thirds or one-half of the forearm.

*Cicatrisation* was regularly satisfactory. The scar on the side of the abdomen was clean and has not inconvenienced any of the patients.

*Sensation.* — This, as a rule, has been good in the radial branch and in the contact surface of the ulna. The outer side of the ulnar stump has shown decreased sensibility, especially noticeable in cases 21, 25, 26, 30, 32 and 37.



Fig. 5 (a, b, c, d). Straight, hinge-like ab—adduction (cases 4 and 6).

*Movement.* — As is well known, the movement of the new hand has generally been described as pure pro—supination, to mention only such writers as SCHLIEPE, OBERLIN, PERKINS. The majority (33) of cases in the present series, however, show that the branches have a straight, hinge-like ab—adduction, which in most cases is possible also when the elbow-joint is extended. All the cases show an opening angle of at least 18 degrees, but in seventeen cases it is 30 to 45 degrees.

*Grasping Power.* — This has been considered rather feeble by some writers (SAUERBRUCH, STEINDLER, and others). It, however, has never been properly evaluated, except in one case (FRAENKEL) where it was two kg. The present writer has used a weighing machine for the evaluation of the grasping power in twenty-three

Table Showing the Results of the Follow-up.

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
Year of Operation	No.	Name	Age	Follow-Up Period in Years	Other Injuries	Length of Stump		Length of Branches	Distance between Distal Ends	Angle in Degrees	Ab—Adduction	Grasping Power, kg, or +, —	Movement × per Minute	Use at Home	Use at Work	Remarks
Group I: Bilateral Amputation. 6 Patients.																
1943	7	E. L.	19	3 1/3	Defect. oculi dx., visus oc. sin. = 0.25	16 sin	8 4	30	+	+	+	6.5	120	+	+	Right Kr made previously (Langenskiöld). Left Kr to be performed soon.
»	8	»	»	»		18 dx	8 4	30	+	+	+	6.5	150	+	+	
»	9	Y. V.	21	»	Defect. oc. sin.	19 sin	9 4	30	+	+	+	7	100	+	+	
1944	23	M. H.	24	2 1/3		24 dx	11 5	20	+	+	+	8	160	+	+	Simultaneous osteosynthesis with good result. Kr-operation preceded by re-ductio cruenta with good result.
1946	35	L. O.	25	1	Pseudarthrosis ulnae sin.	15 sin	8 4	30	+	+	+	+	100	+	+	
»	36	»	»	»		16 dx	8 4	30	+	+	+	+	120	+	+	
»	38	J. M.	35	1		21 sin	11 3.5	25	+	+	+	6	120	+	+	
»	39	»	»	1 1/2	Luxatio inveter. cubiti dx.	17 dx	8 2.5	20	+	+	+	3	110	+	+	
Group II: One Forearm Amputated, the Other Hand Badly Damaged. 10 Patients.																
1943	4	M. T.	28	3 1/2	Only remnant of right hand and part of dig. IV. — Luxatio lentis oc. dx.	25 sin	14 8.5	45	+	+	+	6.5	150	+	+	Letter 2 1/3 years after operation.
»	6	U. S.	21	3 1/3	Styl. p. amp. metac. III—IV man. sin	19 dx	8 6	45	+	+	+	10	190	+	+	
1944	13	E. K.	19	3	» phal. II dig. I—V man. dx.	17 sin	8 6	40	+	+	+	4	120	+	+	
»	21	T. R.	21	1 1/2	Defect. d. II et styl. p. amp. phal. II dig. I et phal. I dig. III man. sin. Defect. oculi sin.	17 dx	8 6					+	60	+	+	
»	26	V. K.	32	1 1/4	On the left hand only part of thumb remaining. Exarticulation of palm at carpo-metacarp. joint defect. oc. dx.	18 dx	8 3						70	+	+	Letter 2 1/4 years after operation.
1945	29	T. M.	23	2	Of the right hand 4 cm of carpus remains. Right eye blind.	25 sin	11 4	20	+	+	+	7.5	120	+	+	
»	30	V. H.	26	2	Of left hand only thumb, remnant of palm, and stiff wrist remain. Blind.	23 dx	12 4.5	30	+	+	+	4	120	+	+	

Group III: One Forearm Amputated, the Other Hand Normal. 26 Patients.

1. Patients Having Lost Their Right Hand. Total Number 15.

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
1946 31	O. R.	22	2			Of right hand thumb and remnant of palm remain. Poor vision.	21	sin	11	6	20	+	+	160	+	+	
1946 37	H. S.	20	1			Right forefinger amputated. Dig. II and V stiff.	23	sin	12	3.5	15	—	6	80	+	+	
1947 43	E. P.	22				Left hand does not work, is quite stiff and partly insensible	10	dx	3	2	35	+			+	+	Still in hospital.
1943 2	M. A.	28	3 1/2				25		14	5	20	+	4	160	+	+	
» 5	T. V.	19	3 1/3				23		11	5.5	33	+	8	170	+	+	
» 10	T. R.	25	1 1/2				25		10	4		+			?	?	
1944 12	H. H.	32	1 1/2				22		10	4		—	±	60	+	+	Letter 3 years after operation.
» 14	B. N.	24	3				30		15	6	30	+	+	180	+	+	
» 15	E. G.	23	1				20		8	3.5		+	+	80	?	?	
» 17	N. V.	22	2 1/2				20		9	4	35	+	6	150	+	+	Uses prosthesis for outdoor work.
» 18	S. N.	20	2 1/2				26		12	5	30	+	6	160	+	+	Letter 2 1/2 years after operation.
» 20	H. V.	23	1				25		10	4		+	+	90	+	+	
» 25	T. A.	35	2 1/3				22		9	4.5	30	+	6	100	+	+	
1945 28	A. L.	23	2				31		14	3.5	18	—	5.5	100	+	±	Uses Kr prosthesis, which works.
» 31	P. M.	35	2				26		10	4	20	+	+	120	+	±	Removed from hospital for use of alcohol.
1946 40	A. R.	35					22		9	4					?	?	Still in hospital.
1947 44	A. M.	8					18		9	3	20	+			?	?	
» 45	K. F.	34					25		10	3	20	+			?	?	— » —

2. Patients Having Lost Their Left Hand. Total Number 11.

1943 1	V. K.	33	7/12				20		11	5		+	5	120	—	—	Letter 4 years after operation.
» 3	H. H.	38	3 1/3				21		10	5	25	+		120	—	—	
» 11	L. A.	20	1 1/2				23		10	6		+	±	80	—	—	Letter 3 years after operation.
1944 16	M. H.	34	Q 1				19		10	3.5		±	3.5	120	—	—	
» 22	U. H.	23	2 1/3				24		12	4	30	+	+	132	+	+	
» 24	T. L.	20	2 1/3				17		8	5	40	+	5	100	—	—	
» 27	T. R.	24	2 1/4				23		12	6	35	+	+	120	—	—	
1945 32	V. K.	21	2				23		10	6		±	±	122	—	—	
» 33	O. S.	14	1 1/2				18		8	3							Removed from hospital for use of alcohol.
1946 41	V. P.	24					20		9	3							Training not yet completed.
1947 42	J. M.	26					26		12	4	30	+	+	80	—	—	

Nearly blind  
Left leg amputated

cases. In seventeen cases the power was at least five kg, once eight kg, and once ten kg. All cases have shown the grasping power of at least three kg.



Fig. 6. Grasping power (case 5).

*Speed of Movement.* — This was also evaluated in thirty-five cases. In twenty-seven of these the claw closed 100 to 190 times in a minute, and in other cases the speed was at least fifty times in a minute.

What has been said in the foregoing shows that the majority of new hands may be regarded as useful with respect to their sensation, the nature and extent of the movement, as well as its power and speed. One more question remains: Have the patients been able to avail themselves of the Kr new hand in daily life?

### *B. Use of the New Hand.*

"Do you use the new hand at home, *i. e.*, when putting on or taking off your clothes, when taking your meals, when smoking, writing, etc.?" Positive answers were given by all except the first patient, although he showed a fairly good left new hand at the end of the treatment. A student who had lost his right hand (case 14) stated that he instinctively used his forceps-like hand for anything. It is interesting to note that those who had lost their right hand used the claw for writing. One patient (case 17) stated that he used his new left hand at home for everything except writing. Female patients used it, for example, when making beds. The best achievement, however, is that three bilateral amputees used their new hands for shaving, putting on and taking off their clothes, eating, etc., all without extraneous help, which



Fig. 7. Grasping power (case 14).

shows that they were able to get along in life quite independently. This can also be seen from the film made by the writer where patients No. 7 and 8 demonstrate all that.

"Do you use the new hand in your vocation?" To elucidate this point, the cases have been divided into three groups in the following.

*Group I: Bilateral Amputation.* — Six cases altogether. The case where both hands had been frozen and where Kr treatment remained merely an attempt is excluded. Likewise, no information is available about the farmer who had Kr claws made on both forearm stumps and who planned working on his home farm. The branches, at any rate, were made (cases 38 and 39). Another farmer, who has one new hand but whose left stump has not been operated on so far, has taken part in farm-work by driving a horse (23). Two patients with new hands on both stumps are now successful house decorators (cases 7—8 and 35—36), one of them planning to continue his studies at the Athenaeum Art College in Helsinki. Patient No. 9, whose right Kr claw was made by LANGENSKIÖLD and left by the writer, stated that he was doing all kind of farm-work at home without prostheses. In winter he wears special gloves made by himself. In the film, this man is presented as harnessing a horse.



a.



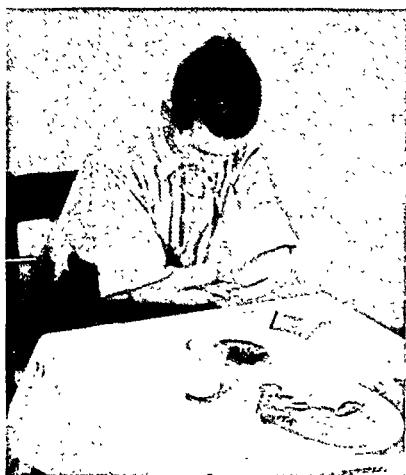
b.



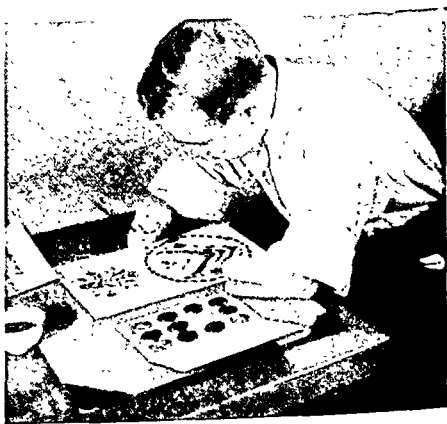
c.



d.



e.



f.

Fig. 8 (a, b, c, d, e, f). A patient who has lost both hands puts his clothes on, has his meal, takes a match from a match-box. He is now a house decorator. (Cases 7 —8. The photographs are reproduced from the film.)

*Group II. Unilateral Amputation, with the Other Hand Badly Damaged.* — Ten cases, six of them also suffering from eye injury, one of the last-named being blind. Patient No. 4 works as a farmer, stating that since he is the only man on the farm he has to do all the work himself. Of the fingers on his right hand only a tip-less ring-finger remains, but he has a new left hand which opens into an angle of 45 degrees and has a grasping power of  $6\frac{1}{2}$  kg. For indoor work he uses the new hand as such, but for outdoor work he has a utility prosthesis. In the film this man is presented as cutting and chopping wood. A smallholder, operated on by the writer a few years ago (case 37), whose right thumb and little finger are stiff and forefinger amputated at the base, stated that the new hand was clearly useful without a prosthesis. Patient No. 6, whose left hand lacks both the fingers and metacarpals III—V, carries on his former vocation as a tractor driver with success. He has a new hand opening with direct ab—adduction into an angle of 45 degrees and moving 190 times a minute. Patient No. 21, whose left palm shows bad cicatrization and whose forefinger and middlefinger and the II phalanx of the thumb are missing, is now a timber-floater at a sawmill without a prosthesis. Patient No. 13, of whose right thumb and forefinger only a little remains, is a shop assistant without prosthesis. The left hand of the blind patient (case 30) had been amputated at the carpo-metacarpal joint so that only the proximal part of the thumb remained, which he was able to press against a splint appliance. He now goes to a commercial school. The film presents him as typing. The injury to patient No. 26 was much the same except that he was not blind. He is now a care-taker, using his Kr hand for writing. One of the patients (No. 31) studies singing at the Sibelius Academy, Helsinki. On his right hand, only the thumb remains, and his sight is bad. Patient No. 29, of whose right hand only a small part of the carpus remains, and whose one eye and one ear are damaged, has no occupation as yet, but has a good new hand.

Thus, all patients of this group stated (with one exception) that they had found the new hand more or less useful in their occupation.

*Group III. Unilateral Amputation, with One Hand Normal.* — Twenty-six cases, which can be divided into two sub-groups according to which of the arms is amputated.

Those who had lost their right, *i. e.*, better hand totalled fifteen. Four cases of this group were particularly encouraging. An intelligent and energetic carpenter (case No. 2), who, after he had lost his hand, passed an examination for a building constructor, now uses his good new hand for designing. A young farmer (case 5), evacuated from the territory ceded to Russia after the war, has a perfectly functioning new hand with a grasping power of 8 kg. He uses it for all sort of work, both with and without a prosthesis, and is therefore very satisfied with the results of the operation. A female patient (case 25) has been able to carry on her work as a dressmaker with the new hand, which, ac-



according to her own statement, had been impossible before the kineplasty. A student of law (case 14), who has a strong forceps hand with ideal function, the stump measuring 30 cm and the branches 15 cm; uses it for everything, instinctively, as he states. Patient No. 17, a farmer, who has an ideal Kr with a grasping power of 6 kg and a speed of 148 times in a minute with ab—adduction, uses it as such for all sorts of small jobs and for writing, but for outdoor work has a conventional prosthesis. A superintendent on a farm uses his Kr (case 12) to some extent, as does a care-taker (case 34), but with a Kr prosthesis.



Fig. 9. A dressmaker who has lost her right hand (case 25).

A former filer (case 28) is now instructor at a machine design course and probably makes some use of his Kr, which, on a 31 cm long stump, has branches opening only to an angle of 18 degrees, a speed of 100 times a minute, and a grasping power of  $5\frac{1}{2}$  kg. It was somewhat surprising to hear that a station official (case 18) who has one of the best Kr new hands (branches 12 cm long, opening angle 30 degrees, ideal ab—adduction 160 times a minute, grasping power 6 kg) uses his claw at home but not in his job. Likewise a worker (case 20) stated that he did not use his claw in his vocation although it worked all right. The only available information on three cases (10, 15, 40) is that one of these patients was a painter's apprentice, one an assistant forester, and one who had been removed from the hospital on account of his addiction to alcohol was sent to prison while the training of the claw was in progress. Cases 44 and 45 are still under treatment.

We find, then, that of fifteen persons who had lost their right hand four use their new hands in their vocation with success and find it useful. Three other patients have found the claw to be of some help. Thus, at least seven disabled persons avail themselves of the claw in

their occupation. On the other hand, two men who have a good Kr. do not use it in their work, and on four no information is available.

Those who had lost their *left* hand numbered eleven. Only one of these uses his claw in his work as such. He is an almost totally blind man (case 24), a basket-maker, who states that the forceps-like hand is absolutely necessary for him in his vocation. The film shows that this man works well with his claw. It was interesting that the man spontaneously asked for the operation. Two watchmen (cases 1 and 22), one worker (3), a fourteen-year-old son of a smallholder, a country housewife (15), and a pupil of a commercial school (32) answered that they did not use the claw in their work. Patient No. 42 has not entered any occupation as yet. Two patients did not answer (11 and 41); the latter has been sent into prison on account of some crime he has committed.

It has to be admitted, then, that in some cases the transformation of the stump has been of little — perhaps even of doubtful — value. Did the operation cause inconvenience to any of the patients? To elucidate this point, the writer made the patients the following question:

"Does the abnormal appearance inconvenience you?" Sixteen patients, *i. e.*, every third of the cases treated, answered in the affirmative, but the remaining two-thirds stated that the claw and a normal stump were equal in this respect.

### *C. Film of the Writer's Cases.*

To supplement his account of the follow-up, the writer has had a cinematographic film made of his cases. The film demonstrates the pure hinge-like ab—adduction, evaluation of the grasping power and of the speed of movement, and the use of the new hand in daily life, with and without prosthesis. The film was shown in 1947 at the congress of the Scandinavian surgeons and orthopedists in Stockholm, at the Stoke Mandeville Hospital, Aylesbury, England (T. Pomphret Kilner, University of Oxford), at the Academy of Medicine, Washington, D. C., at the Nemours Foundation, Wilmington, Del. (A. R. Shands Jr.), and at the Hospital for Special Surgery, New York, N. Y. (Philip Wilson). In 1948 the film has been shown at the Massachusetts General Hospital, Boston, Mass. (Joseph Barr, Wm. Rogers), at the Convention of the American Society for Surgery of the Hand, at the Convention of the American Academy of Orthopaedic Surgeons, Chicago, Ill., at the Children's Hospital, Milwaukee, Wisc. (Walter Blount, Wm. Frackelton), at the Mayo Clinic, Rochester, Minn. (Melvin S. Henderson, Henry W. Meyerding, Ralph K. Ghormley, Mark B. Coventry), at the University of California Medical School, San Francisco, Calif. (Charles O. Bechtol), and

at the University of Colorado Medical Center, Denver, Colo (Atha Thomas).

### Summary and Conclusions.

The writer has since 1943 performed forty-five operations. A cinematographic film of his technics has been prepared by Dr P. G. K. BENTZON, Denmark. 1. *The writer recommends a two-stage operation where all muscles are retained and where the skin can be sutured without tension and the scars and the transplanted skin flap come outside the contact surfaces of the ulnar branch.* 2. *Evaluation of the method must be done on a suitable patient who has a good forceps-like new hand.* 3. *A successful operation results in a new hand that has the best possible appearance, a good sensation, a good blood supply, a sufficient opening angle (about 30 to 45 degrees), a straight, hinge-like ab—adduction when the stump is either flexed or extended, a good grasping power (about 5 to 10 kg), and rate of movement approaching that of the normal human fingers (about 100 to 190 times per minute).* The follow-up was made in 1947. In the whole material the opening angle was at least 18 degrees, but in seventeen cases it was 30 to 45. Ideal, straight ab—adduction was achieved in thirty-three cases. The grasping power was at least 3 kg, in seventeen cases at least 5 kg, once 8, and once 10 kg. The speed of opening and closing the branches was 100 to 190 times per minute in twenty-seven cases and in other cases at least 50 times. 4. *Deserving cases are, apart from the bilateral amputees and the blind, also those whose one forearm has been amputated and the other hand is badly damaged.* All the four patients whose both stumps were transformed into new hands are self-supporting in every respect without extraneous help; two of them are house decorators, and a farmer does all outdoor work on his farm by means of his new hands. Nine men had one hand severely injured, and they now successfully use their good new hands in their jobs. In one such case even a 10 cm long stump has given a good forceps-like hand. 5. *The operation may also be of value in selected cases where only the left hand remains* (the present material contained seven such cases out of fifteen). 6. *The operated amputees have two possibilities: Usually they manage quite well with their new hands as they are, but if they so wish, they are able to use a cosmetic or utility prosthesis exactly as well as the conventional amputees.* — In order to illustrate his results, the writer has prepared

a cinematographic film which he has presented, *e. g.*, at the congress of the Scandinavian Association of Surgeons in Stockholm in 1947, and at the Convention of the American Academy of Orthopaedic Surgeons in Chicago, in 1948.

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## Treatment of Mediastinitis from Perforation of the Esophagus.

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The esophagus in almost the whole of its course stands in relation to various vital organs, and a perforation thereof may easily lead to serious complications, of which the most frequently encountered is infection of the mediastinum. It is especially the posterior part of the mediastinum that is of interest in case of perforation of the esophagus. It is bounded at the back by the spinal column and the prevertebral fascia and in front by the layer of fascia on the anterior side of the trachea. At the level of the bifurcation this latter fascia is connected with the bronchi, and here the downward diffusion of infections is to some degree prevented, a fact which is of some importance as regards the treatment.

According to their *cause* the esophageal perforations are divided into two main groups, one of which comprises those due to malignant tumours and the other those due to foreign bodies and injuries.

Cancer of the esophagus often leads to *spontaneous* perforation, but this usually develops gradually and does not so often give rise to extensive infection of the mediastinum. As it generally denotes a terminal stage of the disease, it is of minor interest from a therapeutic standpoint.

Perforations caused by foreign bodies are of greater practical importance. Most often it is sharp bodies that are present, but blunt objects may also perforate when they have been

lying in the gullet for some time and decubital ulcers develop. In NEUHOF's material, comprising 66 cases of esophageal perforation, 50 per cent were due to foreign bodies. BECKER CHRISTENSEN and JUUL report 223 cases of foreign bodies in the esophagus. Nine of these patients died, three from mediastinitis and two from pyopneumothorax.

The esophagus is seldom subjected to external injuries. On the other hand, internal lesions are more common, especially on probing or attempts to remove foreign bodies. Most often it is the use of instruments "at random" that leads to mishaps. The esophageal wall is thin and easily vulnerable. If stenosis due to old corrosive lesions is present, "blind" probing is especially dangerous, because in case of stricture the lumen is seldom centrally situated and the instrument may easily be caught up in pouches in the wall above the stricture. Injury during esophagoscopy is rare in proportion to the large number of endoscopies that are performed, and such damage occurs chiefly while the instrument is being inserted. The perforation will then occur on the posterior wall at the pharyngo-esophageal junction. (WESSELY reports 7 lesions of the esophagus in 8,667 endoscopies, but the frequency will, of course, be greater when the examination is carried out by an unpractised hand.)

Infection in succession to a perforation *may* be localized to a small area around the esophageal wall, so that we get a "periesophagitis" in the form of a limited infiltration or a small abscess. This is especially the case with the very small perforations, where little infective matter exudes and where there is time for the development of a restricting barrier. But the inflammation will in most cases attain greater extension in the loose connective tissue, and there will occur a diffuse mediastinal phlegmon or a large abscess. In case of greater perforation, where a more extensive infection takes place, the inflammation may spread through the whole of the posterior mediastinum from the throat to the diaphragm in the course of 24 hours.

*The symptoms* vary somewhat according to the extent of the perforation and the height at which it lies. Pain is always present, in most cases severe. It is aggravated by the act of swallowing and is localized to the epigastrium, to the sternum and to the back between the shoulder blades. Emphysema in the neck and in the mediastinum is a characteristic symptom, but may be absent. Fever, leucocytosis, heightened pulse rate and increased

secretion from mouth and throat are commonly noted. If the perforation is small, the symptoms may be of more subacute type, as the infection remains limited in extent. The general condition may be little affected and the temperature only moderately increased. In case of larger perforations, however, the symptoms develop rapidly. There may then soon come signs of collapse, rigor, high fever and often also cyanosis and dyspnea through pressure on the trachea.

A perforation may also lead to mediastinal emphysema of such degree that death may very soon supervene in consequence of the great increase of pressure even before infection has developed.

ADAMS points out that between 6 and 18 hours after the injury there may come a temporary improvement in the symptoms, and that in this period one may get an erroneous impression that the process is in course of regression.

Exudate in one or both pleurae often appears at an early stage. It is usually sterile at first, but may become infected through the spreading of the infection. If the pleura is damaged, there may come pneumothorax and afterwards empyema.

*X-ray examination* may be of great assistance in the diagnosis. Radiological changes indicative of perforation are: Emphysema in the mediastinum and in the soft parts of the throat. A soft-part shadow along the esophagus or an increase of the distance between spinal column and esophagus in cases of circumscribed infection, and increased breadth of the mediastinal shadow in the more diffused infections. If a contrast meal is given per os, the perforation can be directly detected, as the contrast medium presses out into the mediastinum. Water-soluble contrast substance ought to be used when perforation is suspected. By X-ray examination we can further get information as to the presence of air or fluid in the pleura and can detect and locate foreign bodies, if they are roentgen-opaque.

*Treatment.* There are certain measures which must be adopted in all cases of perforation, with or without complications. Peroral ingestion of liquids and food must be avoided. If a duodenal tube can be passed down into the stomach, liquid food can be supplied by that. If this is not feasible, liquids must be conveyed parenterally, or else a gastrostomy must be formed when the treatment becomes more protracted.

Foreign bodies can in most cases be removed by means of an esophagoscope. Esophagotomy will seldom be necessary.



As mediastinitis after esophageal perforation is usually due to infection by one or more of the microbes which occur in the oral cavity and the throat, many of which are penicillin-sensitive, it is natural to expect much from penicillin treatment, both as a prophylactic and as a therapeutic medium. In view of the possible presence of penicillin-resistant microbes it will also, no doubt, be advisable to give sulphonamides at the same time, so long as it is not known what microbes are present in the particular case. With regard to spirochaetes, which often occur in these mixed infections, it was formerly usual to employ arsenic preparations, but these can now probably be replaced by penicillin. The treatment ought to begin as soon as possible.

The treatment has certainly become easier since we got sulphonamides and penicillin, but the estimation of the indications for an operation is no less difficult than before.

Perforations *may* occasionally be seen to heal up without any sign of manifest infection or other complications being observed. Small local abscesses around a perforation may obtain sufficient drainage into the gullet through the perforation, especially if the upper part of the patient's body is kept in a low position, and in this way a surgical operation may become unnecessary. But only extremely few cases take such a favourable course.

Naturally, there will be no doubt as to the necessity of drainage if an inflammatory process is progressive or when we are confronted by a fully developed mediastinal phlegmon or large abscess. But at an early stage it is difficult to come to a decision.

HEAD points out that the surgical problem presented will vary according to the patient's state at the moment of the first examination. The situation is the same as in a case of acute appendicitis. We know that in some cases the inflammation subsides spontaneously. But it is almost impossible to foresee this at an early stage, and if we decide to wait and see, we may often wait too long.

Some authors (including v. HACKER and MARSCHIK) have recommended a "prophylactic mediastinotomy", *i. e.*, opening of the mediastinum as soon as the perforation has been diagnosed, without waiting for symptoms of inflammation to develop. HEAD regards this procedure as justified when the cervical region is concerned, as it is here a relatively small operation, whereas in the thoracic region one ought to be more reserved, since the operation here will be a very serious matter. Against such a

"prophylactic" operation it has been objected that we may come to do direct damage by opening channels for infection in the tissues.

Most of those who have dealt with this subject, however, stress the importance of an *early* operation, even if not made for prophylactic purposes, and these include especially authors who have treated relatively large series of cases.

McGIBBON and MATHER, v. EICKEN and several others recommend observation under close control. This implies frequent recording of temperature and of pulse rate in order to be able to intervene at the slightest sign of progression. During penicillin treatment it may perhaps be permitted to keep the patient under observation a longer time than one formerly ventured to do.

A small and stationary emphysema is not in itself an indication for operation, unless it is accompanied by signs of infection. A large and increasing emphysema, however, may demand a relieving operation when there are symptoms of pressure.

As already mentioned, the anatomical conditions are of importance as regards the choice of a method of surgical intervention. An abscess or cellulitis situated above a horizontal plane through the corpus of the 4th thoracic vertebra can generally be satisfactorily drained by means of a "cervical mediastinotomy", penetrating into the upper part of the mediastinum through an incision along the anterior edge of the sternocleidal muscle on one or both sides, medial to the vascular sheath. In order that the drainage may be effective the patient ought to be placed in Trendelenburg's position. If the inflammatory process is situated lower down, drainage must be effected through a thoracic intervention, usually by means of a posterior mediastinotomy. Portions of one, two or three ribs, in most cases the 7th to 9th, must then be resected posteriorly. The choice of the ribs to be resected depends on the location and extent of the inflammation. The pleura is stripped and the mediastinum approached along the spinal column.

Pleural exudation should be treated by aspiration and injections of penicillin, if infected, but if this treatment is not effective it must be drained according to usual surgical principles. The same applies to the pyopneumothorax that occurs in consequence of perforation of the pleura.

*Prognosis.* PHILLIPS cites what is said by BROYLES in LEWIS'S "Practice of Surgery" in 1930: "Rupture or perforation of the

esophagus results in a mediastinal infection, which is fatal", and by TOREK in NELSON'S "Loose Leaf Surgery": "If, in consequence of such injury, the mediastinum or pleura is opened, death from infection is almost certain to occur." Both these authors seem to have taken a too gloomy view of the prognosis.

PHILLIPS himself treated 20 cases of mediastinitis after perforation of the esophagus. All the patients were operated upon and three died, but none of those who had been operated upon in the first 24 hours.

PEARSE (1938) collected 110 cases of mediastinitis arising after suppurative processes in the throat. In 64 of these cases the mediastinitis originated from perforations of the cervical part of esophagus. The mortality was 56 per cent. Of 33 patients operated upon 9 died; of 31 not operated upon 27 died.

HEAD (1938) assembled from the literature 72 cases of esophageal perforation, all occasioned by foreign bodies. The total mortality was 39 per cent. 26 patients, however, had only a slight infection (local periesophagitis or a small cervical abscess, which was drained into the esophagus) and they recovered without operative intervention. 13 patients had an acute diffused mediastinitis and all of them died, while 11 had a large mediastinal abscess and 2 of these died.

All these series of cases were treated before penicillin and the sulphonamides came into use, and there is reason to believe that these remedies have led to a considerably improved prognosis.

ADAMS (1946) reports from the Lahey Clinic 7 cases of mediastinitis after perforation of the esophagus, treated by mediastinotomy, penicillin and sulphadiazine, and all the patients recovered. DORSEY (1948) reports 4 cases which were treated with penicillin, 3 of them also by mediastinotomy, all four patients being cured.

Generally speaking, the prognosis is better in case of perforation of the cervical than of the thoracic part of the esophagus. The latter lies deeper and is more difficult of access, both for diagnostic and therapeutic purposes, and is more intimately connected with heart, vessels and lungs. The prognosis is also dependent on early diagnosis and treatment.

In 1946—47 there were treated in Surg. Dept. B of the Oslo University Clinic three cases of mediastinitis following esophageal perforation, and an account of these cases shall here be given.

*Case 1. No. 3882/46. Woman aged 61. Previously no dysphagia. On 7/10 46 a piece of bone stuck in her throat while she was eating supper. A doctor tried to pass down a stomach tube, but as this attempt failed and she afterwards got severe pain in the throat, she was sent to the laryngological department of the University Clinic.*

She was then looking rather ill. Tp.  $37.3^{\circ}$  C. P. 80. Esophagoscopy revealed a bleeding rupture on the posterior wall of the esophagus. No foreign body.

*X-ray examination:* She was given a tablespoonful of barium contrast, most of which went down into the stomach, while some passed out through a rupture in the posterior esophageal wall just below the introitus and was gathered in a "pocket", which extended downwards to the level of the 4th thoracic vertebra.

There was instituted treatment with penicillin, 15,000 U  $\times$  8, and sulphathiazol injections, 1 g  $\times$  6.

During the evening she had increasing dyspnea, and next morning she was sitting in the bed with groaning respiration and complained of pain in the chest. On the left side of the neck there had developed a tender emphysematous swelling.

About 16 hours after the perforation: *Mediastinotomy. Esophagotomy.* Through an incision along the left sternocleidomastoid muscle there was opened a cavity, which lay behind the esophagus and extended 15 cm downwards in the mediastinum. Pus and remnants of food were removed herefrom by an aspirator. A perforation was found at the junction of the hypopharynx and esophagus. Drainage. A tube was passed through an esophagotomy down into the stomach to supply nourishment. — Blood transfusion.

In the following days the general condition was relatively good. Temp. around  $38^{\circ}$  C, but the pulse very labile: 110—130.  $12/10$  (3rd day): Increasing dyspnea and stitch in the right side of the chest. Dulness and weakened respiration noted over the right posterior surface.

On the same day she was transferred to *Surgical Dept. B.* Was now in rather bad condition, with cyanosis and dyspnea. On puncture of the right pleura 500 cc of turbid exudate were evacuated. Culture: Growth of yellow hemolytic staphylococci. Injection of penicillin: 50,000 U. On same afternoon 250 cc of serous fluid were evacuated from the left pleura. Culture: No growth.

In the following days the abscess was drained by aspiration twice daily, as the patient could not bear to lie with the upper part of the body in low position. From the pus *Esch. coli* and yellow staphylococci were cultivated. The pleura was punctured at intervals of 2 or 3 days and decreasing quantities of exudate were removed. At the same time penicillin was injected. The sulphathiazol treatment was continued for five days, but had then to be discontinued on account of oliguria and slight hematuria. The penicillin injections were continued until  $16/10$ , by which time she was free from fever.

The general condition gradually improved. A radiogram taken on  $7/11$  after injection of Neo-hydriol through the drain in the neck re-

vealed, however, a large abscess cavity in the posterior mediastinum, with its base on a level with the 9th thoracic vertebra. As the secretion of pus herefrom showed no sign of decreasing and as the drainage in the neck was unsufficient, there was on  $^{11}/_{11}$  46 in local anesthesia done: *Posterior mediastinotomy*. Portions of the 8th and 9th ribs were resected at the back on the left side, the pleura was loosened and shoved aside and the mediastinum was opened. Incision on a sound, which was passed down from the incision in the neck. Drainage.

The discharge from the incisions now soon decreased. On  $^{25}/_{11}$  the tube in the esophagus was removed and she was able to drink. During 2 or 3 weeks a little fluid oozed out through a fistula in the neck, which afterwards closed up.

On  $^{19}/_{12}$  46 she was transferred to the laryngological department, where the esophagus was dilated to relieve a stricture just below the introitus. Discharged on  $^{27}/_{12}$  46 after the esophagus had been dilated for passage of sound No. 27. She could then eat ordinary food without difficulty.

*Case 2. No. 1842/47. Woman aged 62.* In her childhood she had got a stricture after drinking lye. On  $^{15}/_8$  47 a piece of eggshell stuck in her throat and she could not after this swallow solid food. On the same day she went to the outpatient section of the laryngological department. An esophagoscope was inserted and encountered a stricture at a distance of 30 cm. No foreign body could be seen. An attempt to pass a sound farther down did not succeed. After the examination the patient vomited a little blood. Shortly afterwards she got severe pain behind the sternum and in the epigastrium and showed symptoms of collapse. After about an hour she recovered and was then sent for X-ray examination. Barium contrast medium, given per os, passed through a perforation in the anterior wall of the esophagus at the level of the bifurcation out into the mediastinum and oozed right down to the diaphragm.

The patient was then admitted to *Surgical Dept. B*. She was pale and ill and had pain in the epigastrium. Temp.  $37.5^{\circ}$  C. P. 80. B. P. 135/65. Otherwise nothing to be noted on general examination, especially, no emphysema on the neck. Blood transfusion was performed and treatment with penicillin, 50,000 U every 3rd hour, and with sulphathiazol, 1 g every 4th hour, was commenced. Trendelenburg's position.

On the following day the general condition was unchanged, but the temperature and pulse rate had risen. *X-ray examination*: The contrast medium was diffused over almost the whole of the posterior mediastinum. Dull percussion sounds over the left posterior surface from the middle of the scapula to the base. On puncture of the left pleura 500 cc of sanguinolent fluid were evacuated. Culture: No growth. Injection of 50,000 U of penicillin.

Twenty hours after the perforation: *Posterior mediastinotomy*, in local anesthesia and  $N_2O$  narcosis with overpressure. Resection of the posterior parts of the 7th to 9th ribs on the left side. The pleura was stripped outwards. The mediastinum was slit up along the esophagus

from the bifurcature to the diaphragm and a quantity of thin, purulent fluid mixed with barium was evacuated. Drainage. After two days the patient was given food through a duodenal tube passed down into the stomach. Both pleurae were punctured, at first every day, afterwards every second day, and 50 to 75 cc of serous fluid were removed and penicillin was injected. No growth of microbes from the pleural fluid. There were given 50,000 U. of penicillin every third hour in the first 10 days and 20,000 U. in the next four days. The sulphathiazol treatment was continued for 13 days.

The general condition rapidly improved. The temperature was slightly elevated, with some few peaks in the first couple of weeks on account of retention in the wound cavity. She was quite free from fever after three weeks. Through the drainage large quantities of purulent fluid, mixed with contrast medium, were discharged, as well as much mucus. The discharge decreased by degrees and had entirely ceased one month after the operation. The duodenal tube was removed some days later, and she began to drink. There was then no sign of fistula from the esophagus.

*Esophagoscopy* in the laryngological department on  $\frac{3}{10}$  revealed a stricture of the lumen about 38 cm from the denture. On the following days this stricture was dilated. When discharged on  $\frac{13}{10}$  47 she could swallow ordinary food without difficulty and her general condition was good.

*Case 3. No. 2046/47. Woman aged 52.* When she was two years old she drank lye. Since then the gullet has been narrow. On  $\frac{20}{8}$  47 some food got stuck in her throat. On  $\frac{21}{8}$  a physician tried to insert a stomach tube. On  $\frac{22}{8}$  she was esophagoscoped by an oto-laryngologist, who tried to pass a sound down the gullet, but the attempt failed owing to lack of good instruments. After this she felt ill, had pain in the chest and dyspnea. On the same day she was admitted to the laryngological department of the University Clinic. She was now looking rather ill and was short of breath. Temp.  $37.9^{\circ}$  C. P. 100, irregular. Dry tongue. On the neck a distinct emphysematous swelling, mostly on the left side in the supraclavicular region. Over the heart was heard a sharp, crackling murmur. Otherwise nothing to note on general examination. Penicillin treatment was instituted, 30,000 U every 3rd hour.

On  $\frac{23}{8}$  the temperature had risen to  $38.6^{\circ}$  C. and the pulse rate to 120. *X-ray examination of thorax:* Emphysema in the soft parts of the neck and in the mediastinum and a little fluid in the left pleura. Contrast examination of esophagus: Stricture at the level of the 9th thoracic vertebra. No contrast substance outside of the esophagus. *Esophagoscopy:* Just below the introitus somewhat backwards on the left side was seen a pea-sized defect in the mucous membrane, wherefrom there oozed a little blood and dirty-coloured fluid mixed with air. 30 cm from the denture is found a stricture, where there lay remnants of food, which were removed.

The patient was transferred to *Surgical Dept. B* on the same day. In local anesthesia: *Incision.* Through a slit along the sternocleidomastoid muscle on the left side the esophagus was laid bare. The tissue

was edematous, with turbid exudate along the esophagus and the vascular sheath. Drainage. Bacterial examination of exudate: *Proteus vulgaris* and staphylococci.

The patient was placed in Trendelenburg's position. Penicillin: 50,000 U every 3rd hour. Parenteral administration of liquids. On the following day a gastrostomy a. m. Witzel was made. General condition improved.

*X-ray examination* on  $28/8$  showed increased quantity of fluid in right pleura, a little fluid in the left pleura and an increase in breadth of the mediastinal shadow, which bulged out especially on the right side. Puncture of right pleura: 450 cc of serous fluid. Injection of 50,000 U of penicillin. Bacterial examination revealed no growth.

In the following days rise of temperature and signs of basal pneumonia on the left side, which regressed after sulphathiazol had been given in addition to the penicillin treatment.

*X-ray examination* on  $1/9$ : Further increase in breadth of the mediastinal shadow, especially over the 9th costa on the right side. There were also seen clinical signs of downward diffusion of the infection, since from the incision on the left side of the neck a drain could be passed downwards and over to the right into the upper part of the mediastinum. Herefrom a large quantity of pus and mucus was evacuated. Later *X-ray examinations* showed decreasing breadth of mediastinum. From  $1/10$  the patient was free from fever, but there came symptoms of bronchial fistula. On attempts being made to wash out the abscess cavity the patient got liquid in the air passages and had a severe attack of coughing when she tried to drink. *X-ray examinations* on  $6/11$  and  $22/11$  revealed a fistula, issuing from the esophagus at the level of the 7th cervical vertebra and proceeding downwards and backwards on the right side of the esophagus into the apical branch of the bronchial tree.

Her condition remained unchanged until on  $12/12$  she was transferred to the laryngological department. Here there was revealed by *esophagoscopy* on  $22/12$  and by *X-ray examination* on  $27/12$  an egg-shaped diverticulum,  $2 \times 3$  cm in size, on the posterior side of the esophagus at the level of the 7th cervical vertebra. A thin fistula led herefrom 4 cm downwards into the mediastinum, without any communication with the bronchus. Further was found a stricture 28 cm from the denture. In repeated operations with use of an esophagoscope the dividing between the diverticulum and the esophagus was removed by scissors and bioscopy forceps and through diathermic coagulation, and the stricture was dilated. On *X-ray examination* on  $27/2$  48 the stenosis was found to have decreased and there was no filling of the diverticulum or fistula.

When she was discharged, on  $6/3$  48, the gastrostomy had been closed and she could eat ordinary food without difficulty.

Three cases of mediastinitis due to perforation of the esophagus are described. All three patients had retained foreign bodies. Two of them had drunk lye when they were children, and have since

had symptoms of stricture. In one case the perforation occurred during an attempt to introduce a stomach tube, in the other two cases it arose during exploration by an esophagoscope.

In the first case there developed a large, but circumscribed mediastinal abscess. This was at first drained by means of cervical mediastinotomy, but as it later descended to the level of the 9th thoracic vertebra and as the drainage became unsatisfactory, a posterior mediastinotomy had afterwards to be performed. The patient had also empyema on the right side, which yielded to puncture treatment and injections of penicillin.

Patient No. 2 had a large perforation and got diffuse mediastinitis, which was drained by a posterior mediastinotomy on the first day, with good result.

Patient No. 3 had a small lesion on the wall of the esophagus and there came a circumscribed mediastinal abscess, which was drained from the left side of the neck. This drainage, however, was not satisfactory. The abscess descended and the evacuation proceeded slowly. There came perforation to a bronchus on the right side and symptoms of a fistula between the esophagus, the abscess cavity and the bronchial tree. The fistula afterwards closed up.

All the cases were treated with sulphonamides and penicillin, and we have had the impression that this treatment has been very advantageous. It must be taken into consideration that the two patients who had the most severe infections were over 60 years old, at which age one must expect a high rate of mortality in such a serious condition.

The penicillin-sulphonamide treatment, however, has not been able to prevent the development of a mediastinal abscess in Case 1 or to check the progress of a phlegmon in Case 2, but in these cases we have to do with large perforations, causing extensive infections. In case of such large perforations infective matter will be constantly conveyed to the mediastinum from the esophagus, and it is not reasonable to expect that the penicillin and sulphonamides alone will be able to master the infection, so that surgical intervention with drainage will be necessary. Meanwhile, there is good reason to suppose that the chemotherapy has contributed to keep the infection within moderate limits.

Our experiences have also confirmed the view already mentioned that infections in the mediastinum which are descending deeper than the level of the 4th thoracic vertebra cannot be satis-



factorily drained through an incision in the neck, but must be treated by posterior mediastinotomy.

### Summary.

After giving a brief survey of the clinical features, prognosis and treatment of mediastinitis occurring after perforation of the esophagus, the author reports three cases of his own, which were treated by sulphonamides, penicillin and mediastinotomy with good result. While the prognosis in mediastinitis was formerly very unfavourable, the case histories published in recent years seem to show that an essential improvement in this respect has taken place since the use of sulphonamides and penicillin has been adopted in the treatment. Meanwhile, it is not likely that these remedies will render surgical intervention superfluous.

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From the Apelviken Coast-Sanatorium, Varberg.  
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## Tuberculosis of the Greater Trochanter and Trochanteric Bursae.

By

ALBERT AHLBERG,

M. D.

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Affections in the region of the trochanter major are relatively rare, but reading what has been written on the subject in the literature we find that this region may be the seat of inflammation of various types as well as of tumors. There are cases described of peritrochanteric bursitis, bursitis with osteitis of the underlying greater trochanter, typhoid osteitis, tuberculosis of the greater trochanter, and pretrochanteric bursae, Brodie's abscess, osteitis fibrosa cystica, chondroma, giant-cell tumor, myeloma, sarcoma, and other diseases.

As regards tuberculous osteitis and bursitis, there are not many reports on cases of this condition, although it probably is the commonest disease occurring in this region.

That a tuberculous process may develop in the greater trochanter is not a matter for surprise in view of the high degree of vascularization in this region, a condition which has been exhaustively described by NUSSBAUM. Opinions differ as to whether bursitis or osteitis of the greater trochanter is the primary lesion. MARIQUE, WIETING and DONOVAN, among other authors, consider that the osteitis is the primary lesion and the bursitis secondary to this, while KISELEV, and EVANS, for instance, hold that the bursitis is the primary lesion. MELTON is of the opinion that, as a rule, this question cannot be decided with certainty. WIETING states, however, that if no communication between the osteitis and the bursa can be proved this must be due to the fact

that the communication has been interrupted after having been present before. Undoubtedly, the question may be very difficult to settle in the majority of cases, but in the present author's opinion both alternatives may exist. Osteitis in the greater trochanter without any pathologic changes in the bursa and without any microscopic evidence of such a process may be observed at operation. But on the other hand, a process limited to a bursa without any osteitis or defect in the underlying bone is also to be found. Bursitis in this region may also arise from abscesses in the spine or from a process in the bones of the pelvis. Thus we can have a primary or a secondary bursitis as well as a primary or secondary osteitis of the greater trochanter. If both processes are simultaneously present it is often impossible to decide where the process originated.

A large number of bursae have been described in the region of the greater trochanter. The bursae of special interest in this connection are the bursa between the gluteus maximus muscle and the postero-lateral surface of the greater trochanter, the bursa between the ilio-psoas muscle and the ilio-femoral ligament which is often in direct communication with the hip-joint, and the ischio-glutealis bursa.

When these bursae are infected their size increases, their walls become thickened and form part of the abscess wall. They sometimes reach a considerable size and may extend under the gluteal muscles and around the greater trochanter. With regard to osteitis, this may occur either as osteoperiosteal caries, which could be secondary to a bursitis, or else as actual foci in the spongy bone or adjoining the neck or shaft of the femur.

A characteristic feature in the history of the patients is that they have had vague symptoms such as pains and stiffness in the region of the hip-joint over a shorter or longer period with sometimes free intervals lasting for years. The affection can thus last for many years. In some of these cases roentgen examination yields the first evidence of the disease. In other cases an abscess, with swelling, local reddening of the skin and increased local temperature in the region of the greater trochanter gradually develops. The skin gives way and pus escapes, and a sinus then generally forms; this, however, often heals again after a time. This process may be repeated several times at intervals of months or years, and the patient does not seek medical advice. It may also happen that he consults a physician, who opens the "boil", with

the same subsequent result. Complete and final healing after the abscess has been emptied and the sinus closed may also occur.

Examination of these patients reveals that the pains occur in the region of the greater trochanter while in coxitis they occur more towards the medial aspect. In trochanteritis, the patient does not experience pain when the leg is thumped in a longitudinal direction but when it is a case of coxitis he does do so. In the case of the latter disease also, there is definite limitation of all movements as well as an atrophy of the muscles, which is more rarely found in trochanteritis. In those cases where there is swelling over the greater trochanter or an abscess with reddening of the skin the diagnosis presents no difficulty. One ought, however, to bear in mind that in the majority of cases the affection is of a tuberculous nature and that it must be treated as tuberculous after histologic or bacteriologic identification.

The X-ray picture shows, in addition to decalcification, either a subcortical focus or caries with small defects in the cortical outline. Sequester-like calcareous shadows in the soft tissue are often seen outside the greater trochanter. According to STRACKER, because of the tuberculous process in the bone, the tendons have loosened from their insertion on the greater trochanter, with the result that a small necrotic bone fragment together with a small piece of the necrosed tendon works loose. These bone fragments later may become embedded in fibrous tissue in the same way as occurs with ordinary sequestra.

In the material at the Apelviken Coast-Sanatorium, from the year 1928 to the middle of 1947, there are 127 cases of tuberculous bursitis and osteitis in the region of the greater trochanter, constituting 1.3 per cent of all cases of bone and joint tuberculosis admitted to the hospital during the same time. Three cases with a septic process of the greater trochanter were also encountered.

(WASSERSUG, 18 cases (1.8 per cent), SVEN JOHANSSON (2.33 per cent), PACINI and ZANCHERI, 34 cases (1.07 per cent), MELTON, 21 cases (1.5 per cent).) Cases have also been published by MEYERDING and MROZ (19 cases), KISELEV (7 cases), DONOVAN, BERGK, VON SASSEN (5 cases each), CLOPTON (3 cases), TEALE, PEABODY, PERRIN (2 cases each), and SATTA, HAUSER, TIXIER, KEITH, SWINDT, THURSTON, STRACKER (1 case each).

In the accompanying table it will be seen that the majority of the patients were between 20 and 45 years old. The youngest patient was 3 years and 10 months old and the oldest 64 years old. There were 83 men and 44 women.

Table 1.

Age	Men		Women		Total	
	Right	Left	Right	Left	Right	Left
3 yrs. 10 mths. . .	—	—	1	—	1	—
5—10 yrs. . . . .	3	1	1	—	4	1
10—15 yrs. . . . .	2	1	—	—	2	1
15—20 yrs. . . . .	2	6	4	1	6	7
20—25 yrs. . . . .	7	9	3	3	10	12
25—30 yrs. . . . .	2	2	5	5	7	7
30—35 yrs. . . . .	8	5	1	6	9	11
35—40 yrs. . . . .	4	8	1	2	5	10
40—45 yrs. . . . .	2	7	3	1	5	8
45—50 yrs. . . . .	4	—	1	1	5	1
50—55 yrs. . . . .	3	1	2	—	5	1
55—60 yrs. . . . .	3	1	1	1	4	2
60—65 yrs. . . . .	2	—	—	1	2	1
Total	42	41	23	21	65	62 = 127

WASSERSUG states the average age in his cases to be 25.5 years, and considers the disease to be commonest in young adults. MELTON mentions 34.5 years as the average age, and in the opinion of VON SASSEN persons between 20 and 30 years of age are the most susceptible.

As has been mentioned above, the disease may appear as bursitis or osteitis of the greater trochanter, or as a combination of both these conditions. This localization can be a solitary tuberculous manifestation, the only one that can be demonstrated at the time, but it can also occur at the same time as other tuberculous foci in the body. As is seen in table 2, 14 patients had other foci of tuberculosis before the appearance of the process in the greater trochanter. In 44 cases (34.9 per cent) there were at the same time as the trochanteritis other tuberculous mani-

Table 2.

Sex	Other tuberculous foci before trochanteric process	Other tuberculous foci concurrently with trochanteric process	Other tuberculous foci subsequent to trochanteric process
Men .....	8	30	15
Women .....	6	14	5
Total	14	44	20

Table 3.

Sex	Tuberculous coxitis in hip-joint on same side as trochanteric process			Tuberculous coxitis in hip-joint on other side		
	Before	Con-currently	After	Before	Con-currently	After
Men .....	—	16	10	—	2	1
Women .....	1	1	4	1	1	—
Total	1	17	14	1	3	1

festations also, in the majority of cases bone and joint processes (not pulmonary tuberculosis). In 20 cases new tuberculous foci were found after the disappearance of the trochanteritis.

The manifestations of greatest interest in this connection is, of course, the tuberculous coxitis. A study of the histories and X-ray pictures in the cases treated for coxitis during the period covered by this investigation (1928 to middle of 1947, 507 cases) yielded the results shown in table 3.

It will be found that trochanteritis with manifest roentgenologic and clinical changes was present concurrently with the coxitis in 20 cases (3.9 per cent), and that coxitis appeared later on in the same leg as the trochanteritis in 14 cases (2.76 per cent). In the latter cases, the interval of time between the trochanteritis and the coxitis was 3—25 years. Thus, among these 127 cases of tuberculous bursitis or osteitis in the greater trochanter, the hip-joint on the same side later became infected in 14 (11.02 per cent).

As regards the treatment of this affection, most authors agree that an operation is necessary. FROEHLICH insists on conserva-

tive treatment while SORREL operates only when the diagnosis is positively established, and NOVÉ-JOSSERAND first tries conservative treatment and only operates when the joint is threatened. ROCHER also advocates operation. In the present material, extirpation of the bursa and an excision of the changed bone in the greater trochanter was the first treatment tried in 20 females and 40 males, and incision, or aspiration of the abscess or curettage of sinuses was done in 24 females and 43 males. Later on, a further 9 females and 18 males were treated by radical operation, which makes a total number of 87 cases thus treated. In the other cases incision and curettages had to be done repeatedly, and in a few cases also greater interferences, which resulted in a healing of the process.

Regarding the cases where coxitis later developed, an incision or a curettage that had to be repeated several times had been performed in 6 cases. In three of them an excision was done at a later stage. After 3 years, coxitis developed. One of these patients displayed evident progression of the osteitis in the greater trochanter at the same time as the coxitis. In another of these cases remains of the process had to be left in the neck of the femur, and in the third case a sequester in the greater trochanter was removed. Extirpation of the bursa and the abscess was done in three cases at the first operation. Two patients healed by first intention. One of these patients got coxitis 5 years later, shortly after pulmonary tuberculosis, and the other got coxitis after 11 years. In the third case excision of a focus in the greater trochanter was done and after 3 years another revision. Three years later he also got coxitis, which was treated by radical operation. An abscess, which communicated with the part of the greater trochanter previously operated on, was observed at the operation.

In the cases where an excision was performed immediately (5 cases), sinuses remained in 2 of them for a long time; these later necessitated incisions and curettages. One of these patients got coxitis after 3 years and the other after 6 years. More extensive interventions had to be done in 2 cases and both got coxitis 8 years later. In a third case, where the focus had been excised, sinuses, which were not treated, arose several times, and this patient got coxitis after the sinuses had been closed for 6 years.

It is impossible to decide with certainty how the coxitis arose in these cases. The process in the greater trochanter may have progressed into the femoral neck and thus have penetrated into the joint capsule and invaded the joint. The process may also have extended to the adjacent attachment of the capsule, or else the bursitis or the abscess, which were often extensive, may have encroached upon the capsule and into the joint, if a communication

between the bursa and the joint was not already present. The interval of time is, however, so long in most of the cases that clinical healing of the osteitis in the greater trochanter could be observed before coxitis was diagnosed. It is possible that in the surgical treatment of a large abscess with many small ramifications around the joint a small part of the abscess wall was allowed to remain in communication with the capsule, this subsequently causing a coxitis. But the most likely assumption to be made is that there may have been a small focus in the head or neck of the femur which arose at the same time as the osteitis in the greater trochanter and then later began to show activity. It may also, perhaps, have been a question of a reinfection. The intervention on the greater trochanter may also have caused a *locus minoris resistentiae* in the hip-joint on the same side.

As to the histologic examination, this was unfortunately not performed in all cases, particularly the earlier ones. Twenty-three female cases and 40 male cases showed histologic tuberculosis and in 2 cases in each of these groups tubercle bacilli of human type were found in cultures from an abscess. In 3 male cases the guinea-pig test was positive. The clinical and roentgenologic diagnosis was tuberculosis in 19 women and 38 men and of these, 15 women and 27 men also had other undoubted foci of tuberculosis.

After the first hospitalization 35 men and 23 women were cured after bursitis or osteitis of the greater trochanter. Ten men and 1 woman had small sinuses with inconsiderable secretion when they left the hospital. Fourteen men and 7 women returned to the hospital. Eight men and 2 women had got coxitis. Of these, one man died of pulmonary tuberculosis. Four men had small sinuses when discharged. Four men, one of whom is still in hospital, and 2 women were admitted for a third time. One man died of amyloidosis. He had sinuses showing copious secretion. One man had developed coxitis. One man and 2 women who had developed coxitis were hospitalized for a fourth time. One of the women died of myocarditis. The other was discharged as cured.

Of the patients who had other tuberculous foci in addition to bursitis or trochanteritis 26 men and 12 women were discharged as cured after the first period in hospital. Seven men and 4 women had small sinuses. Among the men, two had a process in the os ischii and one in the os pubis. Two men and 2 women are still in hospital. Three men and 2 women with multiple foci died.

Eleven men and 1 woman with fresh sinuses were hospitalized for a second time. The woman was discharged with a scabbed, practically healed sinus. Of the men, 1 is still in hospital, 2 were discharged with slightly secreting sinuses, 5 were cured, and 3 died while in the hospital.



Table 4.

*Patients with Trochanteritis and Bursitis.*

		1 year after dis- charge		2 yrs.		3 yrs.		4 yrs.		5 yrs.		6 yrs.		6—25 yrs.		Infor- mation lacking (on dis- charge)	
		♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀
Cured	I ....	2	1				1	1	1					2		2	3
	II....	1		3	1		1	4	2	2	2			10	4		
Sinus	I ....													1			
	II....			1						1							

I. Submitted to follow-up examination at hospital.

II. Replied to questionnaire.

Three men and 1 woman were hospitalized for a third time. One man died and the others were discharged as cured. Finally, of these, one man was admitted to the hospital a fourth time and died on this occasion. Ten men and 3 women thus had died during the different hospital periods, and one man among these only had an osteitis of the greater trochanter, with running sinuses.

At a follow-up examination of the cases, the patients who were not examined at the hospital answered a questionnaire, supplying information as to whether they were cured since they left the hospital, whether they had been treated at another hospital for this or any other tuberculous disease, and whether there was any limitation of the movements of their hip-joint.

One man had died of pulmonary tuberculosis, 15 patients did not answer the questions or were not examined. In the following tables the result can be seen.

Two women and 3 men left the hospital as cured less than one year ago, 1 man had a small sinus and 2 men and 1 woman are still in the hospital not yet completely cured. Of the patients who answered the questions, 4 men and 1 woman among the earliest cases had on one occasion had a small sinus, which soon healed.

Of the patients who, in addition to bursitis and osteitis of the greater trochanter also had other tuberculous foci, 2 females with healed osteitis of the greater trochanter and 2 males and 1 female with a small sinus, are still in the hospital. Less than one

Table 5.

*Patients with Bursitis plus Trochanteritis plus other Tuberculous Foci.*

		After 1 yr.		2 yrs.		3 yrs.		4 yrs.		5 yrs.		6 yrs.		6—30 yrs.		Infor- mation lacking (on dis- charge)	
		♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀
Cured	I ....	3		5	2	3	1	2				1		2	2	5	2
	II....			1				1				1	3	1	5		
Sinus	I ....			1								1				2	
	II....						1										1

I. Submitted to follow-up examination at hospital.

II. Replied to questionnaire.

year ago, 5 men and 1 woman left the hospital as cured as well as 1 man with a small sinus in the process of healing.

From tables 4 and 5 it will be seen that of the patients who left the hospital more than one year ago and who had bursitis or osteitis of the greater trochanter alone, 38 were cured and 3 still had small sinuses. There was no limitation of the movements of the hip-joint. Of the patients who also had other tuberculous foci without bursitis or osteitis of the greater trochanter 33 were cured and 3 had sinuses. As to the cases with sinuses, they were all patients with large abscesses and diffuse osteitis of the greater trochanter, who had been operated upon several times and in whom scarred tissue had appeared. Among the sinus cases with other tuberculous foci there were 2 with osteitis of the os ischii and one with osteitis of the os pubis.

It can be unreservedly stated that most of these cases with bursitis or trochanteritis are extremely troublesome to treat, a fact which may be seen from the above report. Particular difficulties are presented by those cases where there are other tuberculous foci in the pelvis or the lower part of the spine and where an abscess has penetrated downwards and caused secondary infection of the trochanteric bursa. In these cases, we encounter the most persistent sinuses, and they are practically impossible to treat radically.

The results would undoubtedly be better if patients with bur-

sitis or trochanteritis alone were treated by radical operation at an early stage. Incision or puncture of the abscess is not sufficient, and repeated interventions of this kind only delay the final radical operation, which consequently is more difficult to perform. Whenever there is an affection in the region of the greater trochanter tuberculosis should be immediately suspected and examinations at once undertaken with a view to establishing this diagnosis so that a radical operation may be carried out without delay. By doing this, the course of the disease would probably be shortened, since the process would then not have time to spread to such an extent as to cause difficulties in treatment. The development of coxitis might also be prevented by adopting these measures.

### Summary.

During the period 1928 to the middle of 1947, 127 patients (83 men and 44 women) with tuberculous bursitis or osteitis in the trochanteric region, constituting 1.3 per cent of the cases of bone and joint tuberculosis treated during the corresponding period, were treated at this hospital.

Of these, 14 patients had had a tuberculous infection in another part of the body before the process in the trochanter, 44 had other tuberculous foci concurrently with the trochanteric process, and 20 patients developed tuberculosis in some other part at a later date; in 14 of the last-mentioned cases (11.02 per cent) the later process consisted in coxitis in the hip-joint of the same side.

In 87 cases, extirpation of the bursa and excision of the diseased bone in the trochanter was carried out. Sixty-one men and 35 women were discharged as cured after their first period in hospital. Seventeen men and 5 women had small sinuses in the process of healing. Ten men and 3 women who only had trochanteritis with running sinuses died, 1 of the men dying of amyloidosis.

A follow-up examination of the patients who had been discharged more than one year previously revealed that 71 patients were cured and 6 had small sinuses almost completely healed. Eight men and 3 women who had been discharged less than one year previously were cured, and 2 other men had small sinuses. Two female patients who were cured and 4 men and 2 women with small sinuses were still in the hospital. One man had died of pulmonary tuberculosis and 15 were not examined at the follow-up.

In the author's opinion, a radical operation ought to be the first measure adopted as soon as a diagnosis of tuberculosis has been established.

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## A Case of Internal Biliary Fistula.

By

OLOF JOHANSSON.

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The literature reveals relatively few cases of spontaneous internal biliary fistulae, *i. e.*, pathologic communications between the biliary ducts and the digestive tube, or similar communications within the biliary ducts.

ELIASON (2) reports 5 cases of fistulae in over 15,000 bile duct operations. TRACEY and McKELL jr. (3) found 21 cases of fistulae on the total number of operations at the Lahey Clinic between 1927—42. The number of operated cases was not given. ADAMS (1) found 12 cases in 1,104 biliary operations at the Lahey Clinic during a 4 year period.

The most common fistulae communication lies between the cholecyst and the duodenum, which seems to occur in more than 50 % of the cases (1, 3).

ADAMS reports one case with a fistulae between the cholecyst and the common bile duct. This is the only case found which somewhat resembles the case here reported.

Generally, the diagnosis of internal biliary fistulae can first be made at the operation. Possibly this diagnosis can be made prior to the operation, by, together with other symptoms, establishing the presence of gas in the biliary ducts by means of roentgenogram, or history of passage of gallstones by rectum.

Case number 103/47: a 65 year old male, has always been in good health except for an accident in 1942. No digestion trouble. 1940 or 1941, was ill with high fever, but no abdominal symptoms. Possibly the urine was dark in connection with this illness which lasted two weeks. In 1943 general ill feeling with temperature up to 40° C., which illness lasted 2—3 weeks. The patient recalls severe abdominal pain

at this time, but remembers no details. No further symptoms were noted until November, 1946. At this time the urine began to darken. In the latter part of December the feces was clay colored. First part of January the patient was noticeably yellow. Felt tired, but had no fever or pain. Only slight itching for one week. No urinary trouble. Admitted on January 11, 1947. *Status*: Slight, but noticeable jaundice. *Heart*: O. *Bl. press*: 170/90. *Abdomen*: Soft with no tenderness. Liver not enlarged. No definite resistance to palpation. *Rectal*: Prostate normal. *Laboratory findings*: *Urine*: Albumin: —; sugar: —; urobilinogen: Ehrlich's test ++, Schlesinger +++; urobilin: Hammarsten —; urine diastase 16. *Rest Nitrogen*: 36 mg%. *Serum bilirubin*: Meulen-

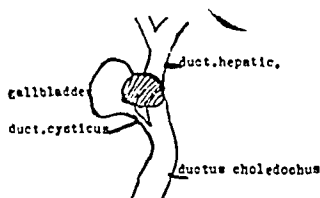


Fig. 1.

gracht 1:40. *Serum citric acid*: 20.0  $\gamma$ /ml. *Serum phosphatase*: 32. *Cholecystography*: The bladder did not fill with contrast. No calculi could be observed with any certainty.

The clinical findings indicated choledochus-occlusion. Since this was a case of painless jaundice (the patient referred to his illnesses from 1940 to 1943 as "influenza", and the details were not made clear until after the operation) one was more inclined to suspect a tumor of the choledochus or of the pancreas.

Jan. 16, operation (author): *Laparotomy + Cholecystectomy + Chole-  
dochololithotomy + Cholangiography*.

Oblique incision below the right ribs. The surface of the liver was definitely rounded, but no indications of an hepatic tumor could be found. The gallbladder was difficult to locate. A very hard structure was felt under the liver, which was first apprehended to be a tumor. Upon loosening some rind-like adherences, both by use of blunt instruments and scissors, a small, shrivelled, crusted gallbladder was revealed, in which was felt a large concrement. Orientation was difficult, wherefore the gallbladder was opened at the fundus and drained of rather light bile, then the stone, which seemed to lie deep in the neck of the gallbladder, was luxated. Upon removal of the stone which was the size of a large pigeon egg, a generous flow of bile issued forth. This appeared very strange, and upon careful exploration toward the neck of the gallbladder, a probe came immediately into the ductus hepaticus and its two trunks. Downward, it entered immediately into the duodenum. The relationship is illustrated in the diagram (Fig. 1).

The stone had lain in a pocket in the gallbladder, which through inflammatory processes adhered to the hepaticus. It had gradually eaten its way through the wall and become an obstruction for the bile passage. Ductus cysticus remained intact. It was very thin and lay

distal to the perforation between the gallbladder and the ductus hepaticus. To insure that there was no more calculi in the choledochus, a cholangiography was done. There was free passage to the duodenum. No contrasting shadows indicating calculi were observed. All remnants of the gallbladder were removed, and the opening in the ductus hepaticus was sewn with isolated catgut sutures, which went well. Two drainage tubes from the gallbladder site and the choledochus. Sutured.

There were no postoperative complications. No bile flow. Patient was discharged Jan. 31, 1947. Serum bilirubin, Meulengracht, was then 1 : 6. The surgical wound was completely healed on March 28, 1947. In 1948, the patient reported that he was in good health.

### Summary.

A 65 year old male, previously in good health. Had at least two acute attacks, which were diagnosed as "influenza". Now was taken ill with painless jaundice. Upon operation was found a fistulae between the gallbladder and the ductus hepaticus, through which a large stone passed into the hepaticus and gradually caused icterus.

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(Head: Professor J. HELLSTROM.)

## Notes on the Anatomy and Physiology of the Thoracic Duct and on the Treatment of Injuries to it,

with reference to three cases of operation injuries and  
one case of subcutaneous rupture.

By

LARS HOLMBERG.

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It is rarely that the surgeon has reason to devote attention to the thoracic duct. This lymphatic duct lies well protected in the body. But modern surgery, when major operations are required in the cervical region and in the thorax, involves the risk that the thoracic duct may happen to come within the area of operation. A lesion of the thoracic duct is a serious complication, as a rule requiring energetic treatment.

At Karolinska Sjukhuset such a complication, with a dramatic course, occurred this year after a cervical operation. Besides this, a subcutaneous injury to the thoracic duct has also been treated. For the treatment of these injuries, it was thought desirable to study similar cases in the literature as well as the anatomy and function of the duct. The result of these studies is submitted herewith.

O. SJÖQVIST (chief of the Neurosurgical Department of Södersjukhuset, Stockholm) has likewise observed three similar operation injuries and has kindly placed the facts in two such cases at my disposal. The third case had previously been published by C. CRAFOORD (chief of the Surgical Department of Sabbatsbergs sjukhus, Stockholm).



## Case-histories.

*Case 1.* Record No. 417/48, Karolinska Sjukhuset. Woman aged 65. Treated at the Radium Institute in April 1947 for cancer linguae with *ligature of a. carotis sin. plus electrocoagulation plus radium.*

Symptom-free until January 1948, when a hard cord, twice the thickness of a finger, was palpated on the left side of the neck. 12. 2. 1948. *Op. I. Radical extirpation* (HELLSTRÖM). Lymphatic glands and m. sternocleidomastoideus on the left side extirpated together. V. jugularis interna ligated and extirpated. 19. 2. Marked reddening round the wound. Skin edematous. Sutures removed. 20. 2. Intensified redness, resembling erysipelas. *Débridement* results in the effusion of a copious amount of greyish-white fluid. Lymph. 23. 2. Copious secretion throughout, bandages changed several times a day. Aggravated general condition. Had merely a slight secretion of urine two days ago. Very considerable loss of chyle. Condition alarming.

24. 2. *Op. II. Extirpation plus tamponade* (HELLSTRÖM). *Débridement* of the wound. The wound cavity filled with greyish-white, thick, membrane-like coagula, resembling clotted milk; in addition, some opalescent fluid. All this is dried. At the bottom of the wound a greyish-white fluid runs out from a short, thin-walled vascular formation, about two mm in width. Impossible to dissect out the duct, and ligature unsuccessful owing to the fragility of the vessel. A gauze tamponade was applied hard against the suspect place and in the remainder of the wound cavity. One tube, suture. In the fluid, on cultivation, staphylococcus aureus and enterococci, sensitive to streptomycin. Patient was given dextran and NaCl. 25. 2. S. R. 115 mm/hour. No distinct chyle in the bandage. 26. 2. Sudan III per os, not visible in the wound. 28. 2. Part of tamponade removed, No chylous secretion. Thanks to blood transfusions and calcium injections, the patient had improved, being less exhausted. 1. 3. Serum albumin had fallen to 5.3, blood calcium to 8.7. Patient had hitherto had a richly albuminous diet, aminosol per os, dextran, etc. 9. 3. Remaining part of tamponade removed. Condition satisfactory. 13. 3. The wound in good healing. 15. 4. Cancer recurrence at posterior margin of wound. New *excision* plus radium. 22. 4. The wound in good healing. 27. 4. Cancer recurrence at anterior margin of wound. Radium. 5. 5. Discharged for return to her home, improved. *Fig. 1.*

*Case 2.* Record No. 7/44, Södersjukhuset. Man aged 27. Previously treated for a left-sided medianus injury. 14. 1. 1944. *Scalenotomy plus division of sympathetic trunk* (SjÖQVIST). Longitudinal cut above clavicle, division of sternocleidomastoideus and omohyoid muscles. In loosening the supraclavicular fat cushion, a large lymphatic vessel, more than a knitting-needle in thickness, was cut: it was possibly the thoracic duct. The vessel was sutured with 3 fine silk sutures. Lymph leaked out during the continuance of the operation, but, when the wound had been sutured after the complete cutting of the trunk below the ganglion stellatum, the wound was dry. 21. 1. Normal healing. No efflux of lymph. 24. 1. *Neurolysis.* 1. 2. Discharged healed.

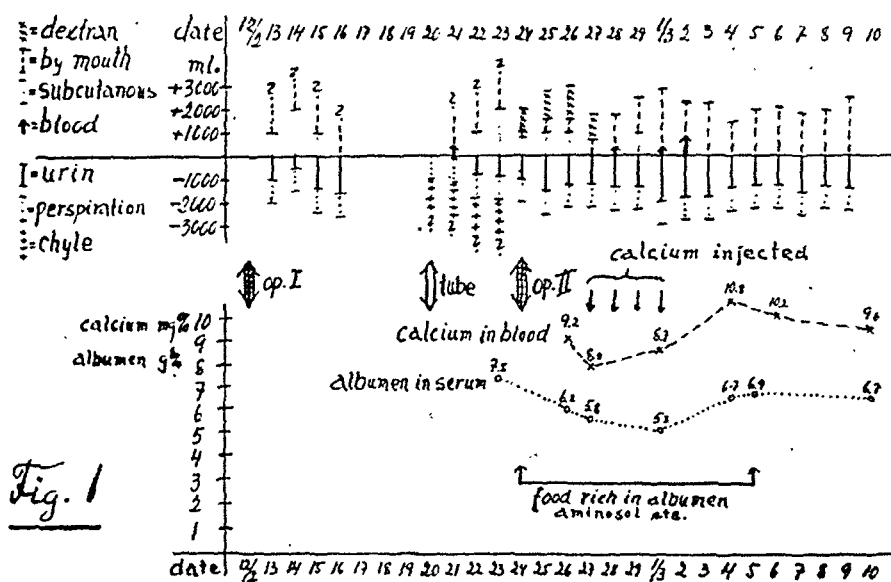


Fig. 1. Fluid balance in case 1.

Case 3. Record No. 1269/47, Södersjukhuset. Man aged 34. Admitted 2.1.1947 because of hypertonia, with headache and scintillating scotoma. 14.1. Op. I. *Splanchnicectomy acc. to Peet on left side* (SjÖQVIST). Resection of 8 cm of 11th rib. Pleura adhered rather firmly, but could be loosened without lesion up to the 9th rib and down to the diaphragm. The 10th, 11th and 12th thoracic ganglia extirpated with intermediate sympathetic trunk. Splanchnicus major somewhat slenderer than usual and lying in fatty tissue close to aorta: 6—7 cm resected. 23.1. Stitch in the chest after the operation. During last few days tired and languid. Second stage fixed for today. Control roentgen, however, showed massive congestion in left pleura. *Thoracocentesis* yielded 1,000 ml milky fluid. During following days repeated thoracocenteses. 8.2. During last few days apparently free from symptoms. The X-ray, however, revealed continued pleural exudate. Discharged for rest at home. 12.2. After a walk felt as if "something had ruptured in the chest". Increasing shortness of breath. 14.2. Marked dyspnea, so that he could not get up out of bed. Admitted again. 15.2. The X-ray showed a large exudate in left pleura. During following days several *thoracocenteses*, altogether 10 litres. 26.2. S. R. 3 mm. Plasma albumin: 5.5. Calcium: 9.6 mgm %. Fat content in chyle 1,990 mgm %. Thoracocentesis today yielded 4.3 litres of chyle. 27.2. Op. II. *Crushing of phrenic nerve* (SjÖQVIST). In the chyle, phosphorus 4.3 mgm%; calcium 7.4 mgm%; fibrinogen 0.03 %; fat content 3,190 mgm%. 28.2. Plasma albumin 4.3. 2.3. Thoracocentesis 4 litres. 3.3. Hematocrit 44 %, CO<sub>2</sub> 58 vol. per cent. Non-protein nitrogen 40 mgm%, chlorine 360 mgm%, NaCl 594 mgm%, plasma albumin 5.5 (albumin 4.1, globulin

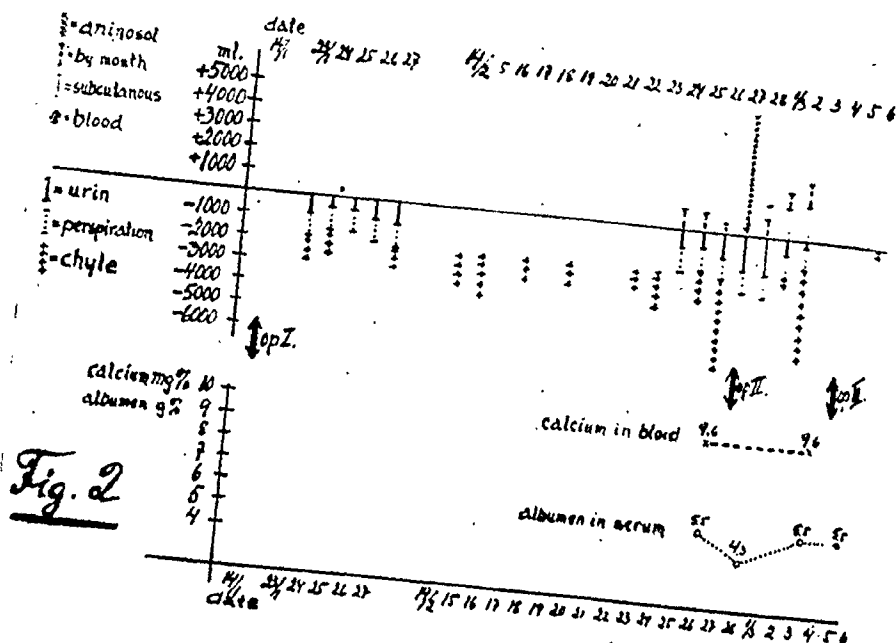


Fig. 2. Fluid balance in case 3.

1.4). Striking change for the worse with marked dyspnea. Transferred to Sabbatsberg Hospital. 4.3. *Op. III. Operation (CRAFOORD)*. Section acc. to method of Crafoord, with extirpation of 8th rib. In the pleura large amounts of slightly sanguinolent chyle. Lung collapsed. Corresponding to a previous operation area, a pleura defect of the size of a child's palm. From this defect thin fluid runs out at the same rate as the dropping from a ureter. Costal pleura flaps are cut. After careful search we find, between the necks of the 9th and 10th ribs, rather near the body of the vertebra, a small fistular opening, half a pin's head in size, from which a stream of watery fluid runs. The lymphatic duct, in which the fistula is like a lateral cavity, is isolated all round and tied with silk centrally and peripherally. After this, all flow of chyle is stopped. A pleural flap is turned down over the fistula opening. In the fixation of the flap, leakage again occurs owing to the needles being stuck into the lymphatic duct, which is distended. New stitching, after which the whole wound is dry. The surface is covered with gel foam, the pleural flap is turned over it. A tube for suction. Suture. 6.3. After the operation 300 ml of fluid had run out into the tube. Puncture of pleura yielded 100 ml of chyle. 2.4. The patient was throughout subfebrile. The X-ray showed an almost complete improvement. Had received penicillin, which was now discontinued. 24.4. Condition satisfactory. Discharged for return home.

Case 4. Record No. 1231/48, Karolinska Sjukhuset. Man aged 27. In 1945, after loading heavy stones on the platform of a motor truck, the patient had a swelling on the left side of the neck, of the same character as now. It healed spontaneously. In 1948, while engaged in

building work, he tried to draw out a thick and heavy plank from a heap of timber. When he had got the plank loose and was still pulling at it, he lost his balance, slipped, but did not fall. He felt a violent jerk in his left arm. After a while he had a swelling on the left side of the neck. Was treated at the out-patient department of Södersjukhuset 5/5—7/5. — S. R. 7 mm. Blood values normal. 7. 5. 48. Admitted to Karolinska Sjukhuset. Had a soft, flaccid swelling over the left clavicle, large as the palm of a hand. Fluctuation at the bottom. Skin normal. *Puncture* yielded ca. 1 ml fluid, which looked exactly like milk, not mingled with blood. 10. 5. Blood chlorides 94 mM. Serum albumin 7.3 %. X-ray examination of the lung showed, on the left side, a chronic tuberculosis of the apex, with calcifications. 13. 5. As the swelling had subsided and had now disappeared, the patient was discharged for return home.

In this case it is conceivable that a tuberculous lymphangitis in the thoracic duct may have rendered the wall so fragile that rupture ensued despite of the presumably slight trauma.

*Anatomy.* To the vascular system lymph is carried from the whole body through the thoracic duct, with the exception of lymph from the right side of the head, the right arm and a minor part of the thoracic wall, which empty their lymph through the right lymphatic trunk, 1—2 cm in length, into the right subclavian vein. In the middle of the seventeenth century these facts were made clear by BARTHOLIN in Denmark and RUDBECK in Sweden. Even at an earlier date certain parts of the lymphatic system had been made known by EUSTACHIO, ASELLI, PECQUET and others; the lymphatic system was known to the scientists of ancient Greece too, as also parts of its function. The most complete anatomical description has been given us by MASCAGNI (1787), whose drawings still serve as a basis for many modern ones, *e. g.* in KILLIAN's work from the year 1940.

The thoracic duct proceeds from PECQUET's cisterna chyli, situated on a level with the 2nd lumbar vertebra. This cistern, however, varies in appearance and size, or may be completely missing. In such cases the lymphatic ducts run direct from the belly up into the thorax. In the lower part of the thorax there are therefore marked variations in the position, number and size of these lymphatic ducts, the place from which the thoracic duct issues, and so forth. As a rule, the thoracic duct is single, but in part or in its entire course it may be doubled (ROUVIÈRE, and others). It receives from different parts a number of larger or smaller lymphatic ducts and sends fine communications to surrounding veins.

In the aortic opening of the diaphragm the thoracic duct lies behind the aorta, close to the right muscular crus of the diaphragm and immediately in front of the spinal column, being fixed to these surrounding parts with thin connective tissue. Above the diaphragm it reaches up to the posterior wall of the esophagus and then follows the esophagus up to Th 5, where it bends off somewhat towards the left, crosses the aortic arch, follows the common carotic artery, dorsally of the latter, up to a level with the clavicle, and then continues in a curve to the left subclavian vein. In the thorax it lies between the aorta and the azygos veins, and may reach up to the sympathetic trunk or the splanchnic nerves on the one or the other side. It is interesting to note that the duct is separated from the esophagus merely by a thin layer of connective tissue, and may thus be injured in extirpation of the esophagus. Such injuries may occur also in extirpation of the sympathetic trunk and splanchnic nerves according to the method of Smithwick or of Peet, etc.

In the cervical region the thoracic duct lies behind the vascular sheath and the vagus, but in front of the vertebral artery and vein. According to ZESAS, it may have a position dorsally of the vertebral vein. The duct is separated from the ganglion stellatum merely by thin connective tissue; as a rule it lies somewhat deeper and somewhat more caudally than the ganglion (MINKIN). Injuries to the thoracic duct have occurred in the extirpation of the ganglion (Sjöqvist and others).

In the cervical region the thoracic duct often divides into several branches, which may either reunite before debouching or debouch separately into the subclavian or different veins. According to PARSON & SARGENT the duct is doubled before debouching in 50 per cent. of the cases; according to CAERIO it debouches as a single duct in 50 per cent., as double in 20 per cent., whilst in other cases it is split up into several ducts, which may be as many as 8 (QUAIN), thus forming a delta.

In persons of the pyknic type the duct, in the cervical region, as a rule reaches up to a level with the subclavian vein, whilst in asthenics it may reach right up to C 5 or 6. The ratio between a high and a low course has been estimated at 2 : 1 (LISSIZYM).

A large number of valves give the thoracic duct a beaded appearance in case of stasis. At the place where the duct opens into the vein there are also two valves, but in 80 per cent. of the cases they are incompletely developed or entirely missing

(KILLIAN). The gross appearance of the duct varies according to the content; when the content is sanguineous it looks like a vein, when it contains chyle it is white or pink in colour; when empty it collapses and may then resemble a nerve.

The innervation is effected via the sympathetic trunk and the splanchnic nerves from the sympathetic system; via the vagus from the parasympathetic system. According to ACEVEDO, KILLIAN and others, stimulation of the sympathetic nerves results in a dilatation of the thoracic duct and of the cisterna chyli, whereas stimulation of the vagus produces a contraction.

The collaterals of the thoracic duct and its communications with the venous system have an important bearing on the question whether the duct can be ligated without risk — a question which has engaged the attention of surgeons for centuries. Injury to the thoracic duct was formerly an extremely serious complication, which in many cases led to death. Towards the end of the 17th century DUVERNEY, FLANDRIN and others had shown that ligature of the duct had no lethal consequences. COOPER nevertheless found that the cisterna chyli ruptured in case of ligature and accordingly in 1798 cautioned operators against it. The discovery of collaterals and communications with the veins brought the question into a new light, and MAGENDIE showed that horses survived a ligature if such collaterals existed. Subsequently, BOEGEHOLD, SCHMIDT-MÜLHEIM, WENDEL, LEE and others made extensive studies of the communications with the venous system. Besides communications with the right lymphatic trunk, there are communications to the azygos veins, the intercostal veins, the vena cava inferior, the renal, iliacal, and, in certain cases, also to the portal veins. Thanks to these communications with the venous system, the thoracic duct can thus be ligated without risk.

A series of investigations on rats showed, according to JOB, that communications with v. cava existed in 48 per cent. of the material, with the portal vein in 27 per cent., and with the renal vein in 8 per cent. All these communications were direct, without lymphatic glands as an intermediate stage. Whether the communication with the renal vein is of any significance as a cause of the rare cases of chyluria has not been ascertained. The communication with the portal vein probably has a bearing on the resorption of fat, as will be shown further on.

The communications with the veins consists of fine vessels, which, however, in case of stasis in the thoracic duct expand and

take over its function. When a ligature is applied a congestion of the lymph can be observed peripherally, so that even the spleen is enlarged (LUCIBELLI), but these symptoms of stasis as a rule disappear after the lapse of 2—3 weeks. In the case of the chyle cysts, which are occasionally found, the cause to these is probably attributable not only to stasis, but also to changes in the collaterals and communications with the veins, possibly also to thromboses in the veins or to local obstructions in the smaller lymphatic vessels of the abdomen.

Whether the thoracic duct or the larger lymphatic vessels can regenerate, is uncertain. On the other hand, the smaller lymphatic vessels are rapidly formed anew, as also the lymph capillaries. REICHERT in 1926 showed that the lymph capillaries were formed anew in granulation tissue within 4 days, and that within 8 days the peripheral lymph stasis was abolished. In experiments on rabbits, he cut the muscles and the periosteum unto the femur, sparing only the femoral artery and vein. These experiments likewise show that, in cases of cancer, it is fundamentally wrong to extirpate the lymphatic glands at a first stage and to defer the excision of the tumour itself until later.

*Physiology.* The function of the thoracic duct, briefly stated, is to convey to the venous system lymph from the body and chyle from the alimentary canal. In this way, according to STARLING and ABDERHALDEN, between 1,500 and 2,400 ml per 24 hours is recovered to the blood. The amounts vary in different physiological and pathological states. In cases of chylothorax HAHN measured 29½ litres in 10 days. SIMON 34 litres in 2 months, LITTLE, HARRISON & BLALOCK 540 litres in the course of well over a year. In the event of a thoracic duct fistula, a loss of fluid amounting to about 1,500 ml per 24 hours is certainly not an excessive computation.

That the lymphatic system as a whole is of vital importance seems self-evident. This was strikingly demonstrated by BLALOCK, ROBINSON, CUNNINGHAM & GRAY in experiments on dogs and cats. In 3 cases out of a total of 74 they succeeded in blocking the lymphatic system completely, almost entirely in 6 and partially in 11 cases. In the cases where the system was completely blocked, the animals did not survive, lymphocytes and acidophils vanished from the blood, the weight rapidly diminished, the peripheral lymphatic vessels markedly dilated, and chyle diffused

into the abdominal organs. In the other cases collaterals developed mainly to the vena cava. In these cases too the lymphocytes and acidophils diminished, though only temporarily. ROUS, BUNTING & HUSTON, LEE and others have likewise shown the diminution of lymphocytes in the blood after ligature of the thoracic duct.

How the lymphocytes are conveyed to the blood-stream is a disputed question. Probably they are carried largely through the thoracic duct, though experiments by BLOOM; SANDERS, FLOREY & BARNES as well as by ADAMS, SAUNDERS & LAWRENCE indicate that there must be also other channels. According to SMITH and WOLIVER, the lymphocytes amount to 90 per cent. of the white cells in the chyle; according to ADAMS, SAUNDERS & LAWRENCE the number ranges between  $9.6 \times 10^6$  and  $92.6 \times 10^6$  per kgm per hour.

The rate of flow in the thoracic duct has been estimated on an average at 30 cm per minute (WEISS), but shows marked variations.

The conveyance of the lymph in the thoracic duct towards the venous system depends on the valves of the lymphatic vessels, the pressure of the interstitial fluid, the muscle-movements, the difference between the positive pressure in the abdomen and the negative in the thorax, the negative pressure in the subclavian vein and, in some degree, also on contractions in the wall of the thoracic duct (ABDERHALDEN, LOE, ACEVEDO and others).

The lymph is derived from the interstitial fluid. As we know, interstitial fluid is formed on diffusion through the blood-capillary wall and during the metabolism in the tissue-cells. Part of the fluid supplied to the interstices is reabsorbed into the vein capillaries together with crystalloids and other diffusible substances. Another part of the fluid, with colloids as well as diffusible and non-diffusible substances, passes through the lymph capillary wall, being thus converted into lymph. The wall of the lymph capillaries is more permeable than that of the blood capillaries. Normally a certain equilibrium is maintained between these different systems.

The amount of interstitial fluid as a rule is small, but may increase in different states, in which cases the amount of lymph likewise increases. This occurs in such cases as physiologic activity of the tissue-cells, diminution of the osmotic pressure in the blood, and greater permeability of the capillary endothelium or cell-membrane in different pathological states. One of these



states is shock, and it has been observed that the flow of lymph in the thoracic duct increases at the onset of shock. The protein content of the lymph at the same time increases (HEIDENHAIN; MANN; MOON, and others). Thus, in a patient with a fistula of the thoracic duct, an incipient shock signifies that the body is losing more protein and fluid than in case of a fistula solely.

The major part of the thoracic duct content comes from the lymphatic vessels of the intestine. BEZNÁK estimated the pressure in the arterial and venous capillaries of the villi as well as in the central lymph capillary and showed that acetyl choline dilated the precapillaries, thereby diminishing the difference between the arterial blood pressure and the capillary pressure, whereupon greater filtration into the lymph capillary results. The flow of lymph in the thoracic duct at the same time increased. Greater tonus in the wall of the thoracic duct owing to excitation from the vagus also plays some part (ACEVEDO). Atropine has a reverse effect on the flow of lymph. By similar measurement of pressure in the capillaries of the villi, KÖNIGES & OTTÓ have shown that lymph is being perpetually formed in the villi and there, as in other tissues, by a process of filtration and reabsorption, corresponding with BAYLISS' and STARLING's view regarding the formation of lymph in the body. On the other hand, it was found that the formation and conveyance of lymph was not affected by intestinal peristalsis or contractions of the villi (BEZNÁK).

From the villi, the lymph is conveyed through the lymphatic vessels of the mesentery to the mesenteric root, where it passes a lymphatic gland station before reaching the cisterna chyli. LEE has shown that there is a marked fall of pressure between the lymph capillaries of the villi and the pressure in the lymphatic vessels of the mesentery (33 and 5.2 cm  $H_2O$ , respectively) as well as in the lymphatic vessel proximal to the cistern (1 cm  $H_2O$ ). The lymphatic glands served as barriers to differences in pressure. On either side of the gland the pressure might be modified without being transmitted past it. In case of ligature of the thoracic duct, the pressure between the cistern and the mesenteric root vessels might be so marked that lymph diffused into the abdomen, as also lymphocytes. The walls of the lymphatic vessels, however, remained intact. In esophagus cancer one often observes a sudden cachexia, which is probably due not only to the rapid metabolism of a cancer, but also to the fact that the body, owing to cancerous invasion into the lymphatic vessels of the abdomen and into the

thoracic duct, is deprived of the nutrient chyle fluid. A stasis of chyle is probably also a contributory cause of the large amount of ascitic fluid found in peritoneal cancer.

Chyle contains between 1 and 6 gm % proteins. The ratio between albumin and globulin was found in DORSEY and MORRIS' cases to be 12: 13, in those of WATSON and FOSTER to be 1.34 : 0.39. The protein content in the interstitial tissue fluid is considerably less than in the lymph within a corresponding area.

Whence do the chyle proteins then originate? The amino acids are resorbed, through the blood capillaries situated superficially in the villi and via the portal vein, into the liver. From the liver the amino acids are either transmitted to the tissue-cells of the body, are built up there, stored or broken down again; or else — presumably the major part —, they remain in the liver, are broken down or built up into higher albumens, especially those of the blood plasma. In liver stasis it has been found that the capillaries of the liver are more permeable by albumen than the other capillaries of the body (EVANS). Even normally part of the albumen presumably passes into the lymph capillaries of the liver and thus into the thoracic duct. Moreover, some of the amino acids are resorbed through the lymph capillaries of the villi and, in this way, direct into the thoracic duct. COTUI *et al.* and SHAFIROFF *et al.* have found that the thoracic duct conveys albumen from the albumen deposits of the body, inclusive of those in the liver. All this may thus explain the abundant content of protein in the chyle. Thus, *in the case of a fistula of the thoracic duct the body loses albumen from the interstitial fluid, from the albumen reserves of the body, from the liver and, in part, from the food.*

MADDEN and WHIPPLE have estimated the protein reserve in dogs to be 1—2 times the normal protein content in the blood. When this reserve has been consumed, the protein content in the blood can be maintained only by the supply of sufficient amounts of albumen of fully adequate quality. In man this can be effected by the supply of aminosol or richly albuminous diet, such as lean cheese, eggs, meat, dry milk diluted with equal amount of water (in which case 4 times as much albumen is supplied as the corresponding amount of ordinary milk, ROSENQVIST). Dextran increases the osmotic pressure of the blood.

The *percentage of fat* in chyle varies, according to DAVIS, between 0.4 and 2.8 cc per 100 cc. According to several authors, 60—70

per cent. of the resorbed fat is conveyed through the thoracic duct.

What then becomes of the remainder? As we know, fat is resorbed in the food as unsplit neutral fat through the lymph capillaries of the villi. Some of this fat is presumably conveyed to the liver through the above-described communication between the lymphatic vessels and the portal vein (JOB). Besides this, some of the fat in the food is hydrolysed, absorbed by the blood capillaries in the villi and conveyed to the liver (EVANS). This is probably the reason why the entire amount of fat is not found in the thoracic duct.

The resorption of fat and the satisfaction of the fat requirements of the body are disturbed merely in a minor degree by ligature of the thoracic duct (EVANS; SCHMIDT-MÜLHEIM; LEE). On the other hand, a great deal of fat is lost in case of a thoracic duct fistula.

The *sugar percentage* is the same as in the serum.

The chyle fluid has been examined in several cases of chylothorax and fistulae. CRANDALL, BARKER & GRAHAM found that the protein percentage ranged between 3.19 and 5.28 gmm %. The flow of chyle was 0.93 ml per minute, or 1.38 ml per kgm body-weight and hour. After a heavy meal the flow increased to 3.9 ml per minute. Fatty food tended to increase the rate of flow to double, whereas drink had no marked effect. Massage of the abdomen, increased peristaltic movements of the intestine or intensified muscular work did not raise the flow of chyle. Sudan IV, administered per os, was found in the chyle after the lapse of 1 hour, 27 minutes.

The lymph in the thoracic duct contains also *fibrinogen*, but in smaller amount than in plasma. The number of *thrombocytes* is likewise smaller: the lymph therefore coagulates more slowly than plasma. The lymph coagula consist of fibrin mingled with fat and are pitted with larger or smaller cavities, containing thinly flowing chyle, with a milky appearance. Evidently, these coagula are merely of slight importance for the spontaneous healing of a thoracic duct lesion. (*Case 1.*)

Chyle also contains *calcium* (LOE and others). In *case 3* the calcium content was 7.4 mgm %. Chyle moreover contains *cholesterol* (DORSEY & MORRIS), *phosphatases*, *vitamins*, etc. JOHNSON & FREEMAN found in dogs a *hemolysing substance* in the lymphatic vessels: in minor amount in the thoracic duct, especially after a richly fatty meal. Whether the said substance

is of any importance in man is uncertain. No case of hemolysis after infusion of chyle has been reported.

*Clinical findings.* The chief symptom of a thoracic duct affection is secretion of chyle inwardly towards the body-cavities or outwards. If this symptom is lacking, the pathological states in the thoracic duct as a rule can scarcely be diagnosed. Chyle secretion outwards occurs in cases of open traumatic injuries, whilst secretion into the body-cavities occurs far more frequently in connection with internal affections than with traumatic injuries.

Chylothorax is the principal symptom of internal affections of the thoracic duct (WATSON & FOSTER; WESSEL; YATER; FORBES, and others). Thus, chylothorax may develop in connection with benignant or malignant tumours in the thoracic duct, in cases of tuberculosis, of multiple thromboses in the veins, especially in the subclavian and jugular veins (BLALOCK *et al.*), in about half the cases where vena cava superior had been ligated (BLALOCK *et al.*), in connection with lymphangites or aneurisms in the thoracic duct, filariasis, liver cirrhosis or cardiac insufficiency (KILLIAN, MOST and others).

The traumatic ruptures may be subcutaneous or intrapleural, and are due to indirect lesions, *e. g.* in connection with fits of coughing (KILLIAN and others), contusion of the neck or thorax, or sudden straining of the spine (BROWN). In *case 4* rupture probably ensued in connection with a jerk in the left arm, resulting in a subcutaneous effusion of chyle. (As the X-ray revealed apical tuberculosis in the left lung, it is possible that the thoracic duct was tuberculously affected and thus fragile, with rupture in consequence of a probably slight trauma.)

The commonest causes of thoracic duct injuries are, however, direct being either due to projectiles or cutting objects, such as knives, fragments of fractures, etc., or else ensuing at operation.

Injuries to the smaller lymphatic vessels as a rule, so far as we know, are of but little importance. Sometimes, however, they give rise to so-called "seromata", which delay the healing and may become infected. Similar effusions of lymph may occur subcutaneously in case of injuries which fall in the skin tangentially. Injuries to the thoracic duct or to its afferent lymphatic vessels are of so much greater importance.

At operations the cervical thoracic duct may be injured in extirpation of tuberculous or cancerous glands (ZESAS and others)

— see *case 1* —, extirpation of an aneurysm, of a malignant struma, of the ganglion stellatum (SJÖQVIST, see *case 2*), in resection of the 1st rib, scalenotomy, operations for torticollis, etc.

The intra-thoracic part of the duct may be injured in costal resections (SMITH & WOLIVER), sympathectomy according to the method of Smithwick (WHITCOMB & SCOVILLE), or of PEET (PEET & CAMPBELL, CRAFOORD, see *case 3*) as well as in extirpation of the esophagus (LOE; PUESTOW & CHESSE), lobectomy etc.

The injury may be discovered at operation, but as a rule manifests itself at a later stage. Injury of the intra-thoracic part of the duct at first gives rise to chylomediastinum, which eludes diagnosis, but may be detected on the roentgen picture by an alert operator as a shadow beside the spinal cord (BROWN). As a rule after 4 days, but sometimes not till after the lapse of up to six weeks, the chyle fluid breaks through the arrodged pleura, suddenly giving rise to symptoms of pressure from the thorax (LITTLE, HARRISON & BLALOCK, and others). Chylothorax may be unilateral or bilateral, and may possibly be combined also with chyloperitoneum.

When in doubt about the diagnosis, the chyle fluid may be stained with fat-coloring dyes. If the fluid is allowed to stand, it will separate into an upper creamy layer, an intermediate layer of milk and a layer of sediment at the bottom. According to KILLIAN, it can, in certain cases, be distinguished from a tumour exudate by the fact that chyle never contains cellular fragments.

*Treatment.* The consequence of a thoracic duct fistula, whether inwardly towards the body-cavities or outwards, is usually a rapid loss of fluid, proteins, salts and fat. If the patient is left without effective assistance, the result is a rapid drying and inanition with a bad general condition, headache, etc. The treatment should be concentrated primarily against the loss of chyle, secondarily against the injury to the thoracic duct.

The therapy must be energetic. The loss of albumen should be replaced by blood or plasma transfusions, by richly albuminous diet, or by the supply of aminosol. The osmotic force of the blood can be maintained by infusions of dextran. The salt deficit should be replaced. In the case of a protracted fistula, vitamins should also be supplied (WATSON & FOSTER).

The supply of fat should be reduced to a minimum, and atropin may be tried in order possibly to reduce the flow of chyle.

Relieving thoracocenteses must sometimes be resorted to two or three times a day. A sterile chyle fluid may be supplied intravenously, as was first done by OEKEN in 1908 (the case had a lethal termination), afterwards by BAUERSFELD; DORSEY & MORRIS; WHITCOMB & SCOVILLE; LITTLE, HARRISON & BLALOCK; SMITH & WOLIVER. A case of mortality in connection with chyle transfusion has been reported by WHITCOMB & SCOVILLE. — LITTLE *et al.* supplied more than 22 litres of chyle to a single patient. PEET & CAMPBELL administered chyle intrasternally.

Before the chyle fluid is administered, it should preferably be kept cold after the supply of a citrate solution, until bacterial tests have given a negative result. SMITH & WOLIVER kept chyle for 4 days without injurious consequences.

Formerly it was considered necessary to *suture* the lesion or to *implant* the thoracic duct in a vein. In practice, however, suture or implantation are delicate procedures. The operation has nevertheless been performed with good effect by DEANESLY (implantation), HARRISON (ditto), CUSHING (suture), SJÖQVIST (see case 2) and others.

In the cervical region, *ligature* of the thoracic duct or, as the case may be, the lymphatic vessel, must now be regarded as the normal procedure. On the neck the incision should preferably be made along the clavicle; the vascular sheath is dissected out, the jugular vein is followed downwards to the subclavian, where one may expect to find the thoracic duct. MINKIN recommends us to follow the vascular sheath upwards until the carotid bends off somewhat inwards and the jugular somewhat outwards. Between these vessels and behind them the crossing lymphatic duct will be found in front of the vertebral vein. LOE recommends that the ends of the thoracic duct should be inserted behind the vascular sheath or in musculature.

Cases with secretion of chyle in spite of ligature have been reported; in such cases it was necessary to reoperate once or even twice before the result was satisfactory (KRON).

After ligature it sometimes occurs that the patient has discomfort from the abdomen, which is probably due to the temporary stasis of lymph. This discomfort as a rule disappears after about a week.

Ligature of the intra-thoracic part of the duct involves a much more serious surgical intervention and in such lesions we are warranted in at first adopting an expectant attitude. BLALOCK

*et al.* succeeded in keeping such a patient alive for over a year. To judge by reported cases, the lesion may evidently heal spontaneously. We are probably then concerned with a minor rupture or injury of a collateral branch. NOWAK & BARTON recommend that an attempt be made to increase the prospects of healing by operation of the phrenic nerve.

Should it be found impossible to maintain the fluid balance and if the leakage does not cease spontaneously, there remains the possibility of ligature even in the intra-thoracic cases. In *case 3* CRAFOORD succeeded in performing the operation. WHITCOMB & SCOVILLE as well as PEET used silver clips in similar operations. BROWN has indicated a possible way of draining the chyle outwards by an incision from the dorsal side, resection of a rib and dissection at the posterior mediastinum up to the injured thoracic duct part.

Should ligature fail in the cervical cases, there remains as a last resort the expedient of *tamponing*. In many cases, however, tamponade has failed (KRON and others). DOBBERTIN's method with fat-free cottonwool in gauze was evidently an improvement. In *case 1* an ordinary gauze tamponade was used with good effect. It is important that the tamponade should be left for a sufficient length of time, at least 8 days.

Evidently, however, some minor thoracic duct injuries heal spontaneously, as in *case 4*.

*Prognosis.* The prognosis for these injuries had previously been considered to be bad, and must still be judged with some caution. For example, the conservative treatment of chylothorax formerly showed a 50 % mortality, the operative treatment 100 per cent. These figures, however, are already antiquated, thanks to modern fluid therapy as well as the development of thoracic and cervical surgery, and we may expect that quite different figures can be recorded in the future.

### Summary.

In this paper the author describes two cases of injuries to the thoracic duct, which had occurred during extirpation of cancerous glands on the left side of the neck and, respectively, scalenotomy plus division of the cervical sympathetic trunk; one case subjected to sympathectomy according to the method of PEET; and one case of subcutaneous traumatic rupture, where, however, it is

conceivable that a tuberculous lymphangitis in the thoracic duct existed simultaneously. In two of these cases the course was dramatic, which occasioned reoperation: in the one case tamponade, in the other thoracotomy with ligature of the thoracic duct. In the third case the injury was discovered at operation, and the two ends of the lymphatic vessels were sutured. In the fourth case the injury healed spontaneously. All these patients recovered, without a continued secretion of chyle.

The literature of the subject is summarized, as regards the anatomy of the thoracic duct, the physiology of the lymphatic vessels and the treatment of injuries to the thoracic duct.

In the event of injury to the thoracic duct or its larger afferent branches, the disturbed fluid balance should be restored, so far as possible, to normal values, which requires an energetic administration of albumen per os and intravenously, a supply of fluid and salts (calcium etc.), and in case of a protracted fistula of the lymphatic duct, the administration of vitamins. The supply of fat should be reduced to a minimum. Atropin may be tried, in order to diminish the flow of chyle.

In addition, the author discusses the question of injuries to the lymphatic vessels. In case of injury to the cervical thoracic duct, ligature is recommended. Should it fail, there remains the possibility of resorting to tamponade, which should then be left undisturbed for at least 8 days. In case of injury to the intra-thoracic part of the duct, an expectative procedure is recommended. Should this not lead to the desired result, a ligature must be made. The ligatures should always be applied both centrally and peripherally of the injury. As a third expedient in cases of injury to the intra-thoracic part of the duct, drainage outwardly according to the method of BROWN may be tried, so far as the position of the injury can be judged. This method, however, is merely of palliative nature, being intended to prevent the formation of chylothorax, with its effects on heart and lungs.

Certain minor injuries probably heal spontaneously.

Thanks to the resources of modern fluid therapy and the development of thoracic and cervical surgery, the prognosis must now be judged as relatively good.

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## Vagotomy, Report on Autopsy Four Months after Operation.

By

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After resection of the vagus nerves peptic ulcer heals with marked regularity as judged by clinical and roentgenologic observations [DRAGSTEDT (1)]. Even though the acid secretion partly returns in the course of 6—12 months, there is, as determined by the insulin secretion test [HOLLANDER (2)], no sign of regeneration of the resected nerves. Fear lest the vagus nerves should regenerate — in analogy with the regeneration of sympathetic nerves — has led to employment of special technical procedures to avoid this [MOORE (3)]. Presumably, it is very rare that there is an opportunity to do autopsy on a patient, upon whom vagotomy has been performed some length of time previously; we have seen only 1 case, published by MOORE (4); a patient died 6 months after operation, from a cerebral vascular accident, and autopsy showed no regeneration that could be demonstrated, of the resected nerves. As one of our patients died from another cause approximately 4 months after vagotomy had been performed, we find that it may be of interest to publish the autopsy findings.

A. M. H. (Case No. 4609/47), a 51-year-old man, who gave a history of dyspepsia from the youth. He had three times been placed on medical management with transitory relief. In 1941 he was operated upon in Germany for perforated ulcer (oblique incision under right curvature). In 1947 symptoms recurred. On June 17, 1947 subtotal gastrectomy

(Polya) was performed; duodenal ulcer was demonstrated. One month after the operation epigastric pain recurred. On December 1, 1947, roentgen examination showed typical peptic jejunal ulcer with hazel nut sized crater (Fig. 1). Ewald's test meal showed no free acid (2 tests); by the insulin secretion test (20 units given intravenously) free acid rose to 77 units, total acid to 92 units. On December 15, 1947 abdominal vagotomy (Dragstedt's technique) was performed; ulcer was demonstrated in the jejunum 2 cm distal to the site of anastomosis; there was a nut-sized infiltrate and the tunica serosa was covered with a whitish coating. Segments, 2 cm in length, were resected from two large nerve trunks and a smaller one. The nerves were simply cut without ligature. The recovery was uneventful. The abdominal pain disappeared immediately after the operation. On the twelfth postoperative day roentgen examination showed no sign of ulcer (Fig. 2) and an insulin secretion test gave no free acid.

For some time following vagotomy the patient was annoyed by diarrhea after each meal, but this gradually changed, so that he had normal stools a couple of times daily. He was able to eat an unrestricted diet. At intervals he was discomforted by pain under the right curvature; this pain had been present since the operation in Germany, and was probably due to neuralgias in the scar from the operation there. He stated that he had become somewhat nervous since the vagotomy, but this condition had been markedly aggravated after an influenza in March 1948. He had a sensation as if the houses closed up when he was walking the street, and might have attacks of cold sweat and wiping; during these attacks he had diarrhea. When he was seen on March 22, 1948 he stated that he was eating a regular diet and had no gastric symptoms. Blood pressure was found to be 130/75. Hospitalization for further examination was arranged. However, private troubles turned up, and on April 4, 1948 he committed suicide by means of sleeping pills, four months after the vagotomy.

April 7, 1948, Autopsy:

Weight 68 kg, length 170 cm, nutritional condition a little below normal.

*Esophagus:* On the posterior surface the right vagus nerve could be traced to 1.5 cm above the cardia, where it ended in a slightly flask-shaped portion (Fig. 3). On the anterior surface the left vagus nerve extended down to 1.3 cm above the cardia, where it ended in a small irregular lump of fibrous connective tissue; in addition, to the right of the nerve trunk there was a thin strand; this anastomosed cranially with the vagus nerve and ended caudally in a fan-shaped area of fibrous connective tissue (Fig. 4).

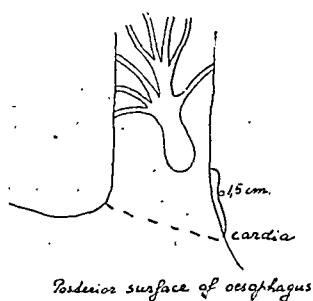


Fig. 3. Posterior surface of the esophagus with the lower end of right vagus nerve.

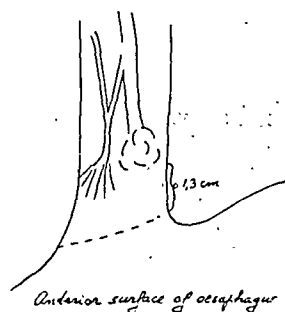


Fig. 4. Anterior surface of the esophagus with the lower end of left vagus nerve.

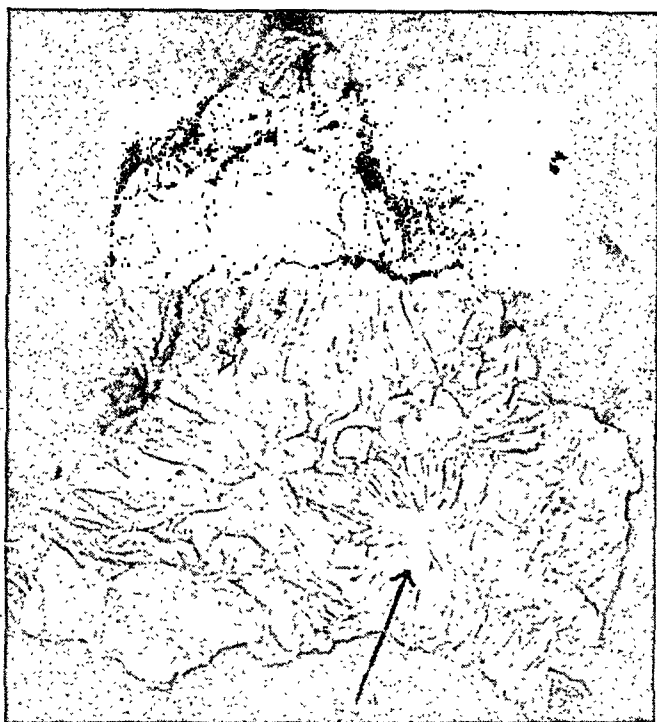


Fig. 5. Peptic ulcer healed.

*Stomach and Small Intestine:* The pyloric portion of the stomach and first part of the duodenum had been resected according to the technique of Polya. Anastomosis had been established to the upper loop of the jejunum. External inspection showed a smooth transition between the stomach and jejunum. Just caudal to the site of anastomosis a slight retraction of the tunica serosa on the posterior surface of the descending portion of the jejunum was seen. The tissue was soft to the touch. When the stomach and jejunum were cut open, a

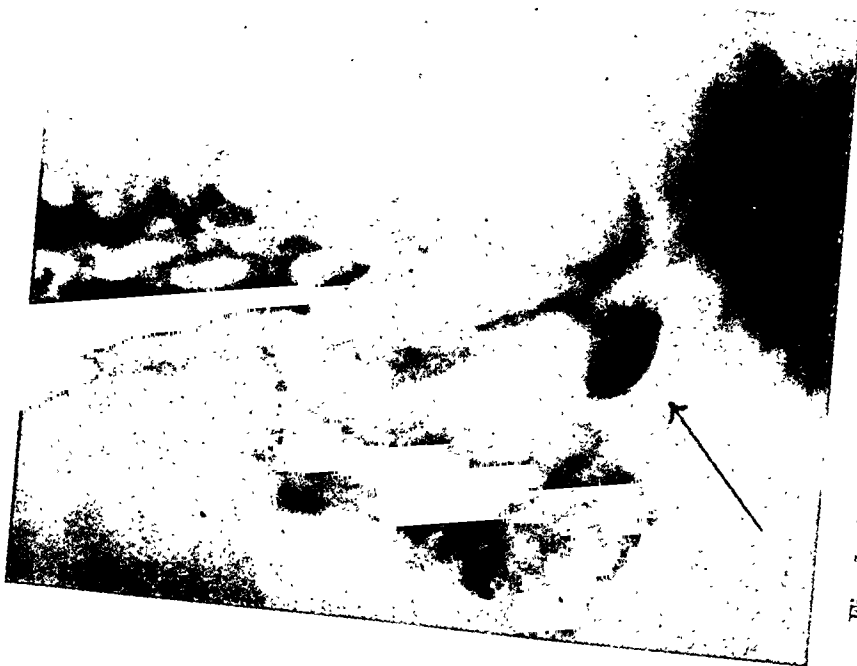


Fig. 1. Peptic jejunal ulcer, before vagotomy.

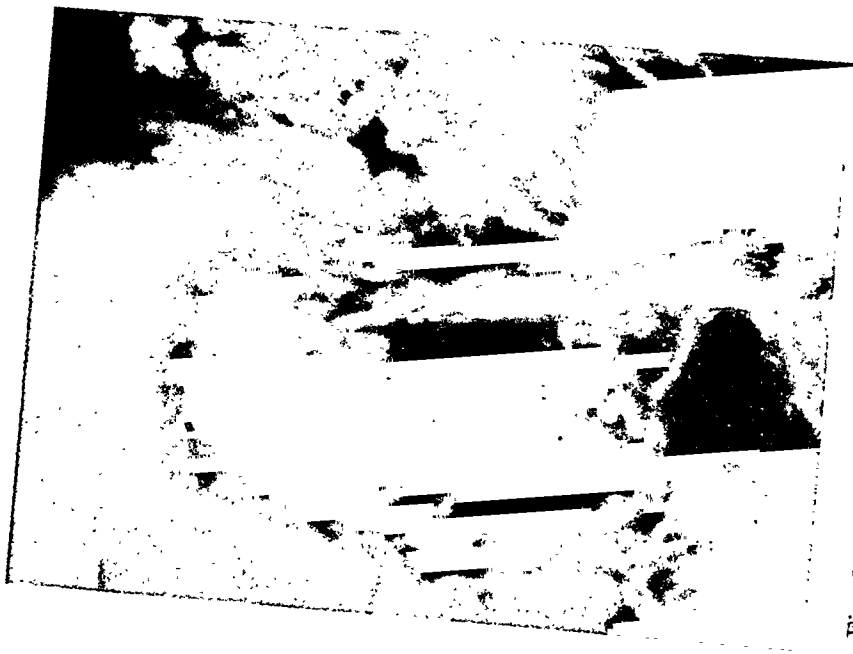


Fig. 2. Ulcer healed, 12 days after vagotomy.

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Fig. 6. Microscopic section of the ulcer. The mucosa regenerated with gland formation.



Fig. 7. Section of lower vagus end. No sign of regeneration.

slight depression in the mucosa, corresponding to the retracted area, was found. The folds of the mucosa were converging towards the site of the former ulcer, but the continuity of the mucosa was not broken, and there were no signs of inflammatory processes in the circumference (Fig. 5).

We shall not describe the other macroscopic findings in detail as they were due to the lethal poisoning.

The findings were as follows:

Gastric resection performed after the technique of Polya.

Vagotomy performed.

Healed peptic jejunal ulcer.

Acute stasis of the organs (due to medinal intoxication).

Bilateral bronchopneumonia.

Atheromatosis of the coronary arteries.

Severe edema and stasis of the brain.

### Histological Examination.

*Section of the Peptic Ulcer:* The mucosa had regenerated everywhere in the ulcer, even though it was lower than the surroundings. The epithelium was cubical, rather irregular. It had developed into short tubular gland formations. The adjacent layers were cicatricial, fibrous with scattered stretches of non-striated musculature. As a whole the intestinal wall here was thinner than normal. There were scattered infiltrates of plasma cells and lymphocytes (Fig. 6).

A longitudinal section of the vagus ends and esophagus was made. The vagus ends were embedded in cicatricial connective tissue infiltrated by chronic inflammation, forming a fine capsule around the cut nerves. The nerve strands were somewhat irregular and plump, but the architecture of the nerve was otherwise well preserved (Fig. 7).

*The Esophagus,* transected caudally to the vagus nerves showed natural conditions. Only a single, very slender nerve strand could be demonstrated in the tunica adventitia.

It has thus been possible to demonstrate both macroscopic and microscopic healing of the ulcer, and no signs of regeneration of the vagus were found.

It has been feared that following vagotomy a "nervous load" might arise owing to the blocking of the impulses from cerebrum, or that symptoms from other fields of the vegetative nervous system might develop. It cannot be categorically dismissed that such circumstances may have played a rôle in this patient. He was said to have been psychically normal prior to the gastric resection; during the war he worked in Germany and had been exposed to several air-raids, which got on his nerves. His complaints after the gastric resection made a rather neurotic impres-



sion, so that we were surprised at the presence of peptic ulcer. Thus he was not an ideal subject for vagotomy. After the operation his nervous complaints were aggravated. The stomach did not trouble him any more, but he had attacks of tremors, anxiety, cold sweat, and diarrhea. It is an interesting thought that these attacks were perhaps equivalents of his previous gastric symptoms, or parallel vegetative disturbances, now with a predominant sympathetic touch. As already mentioned his blood pressure was normal after the vagotomy; it has, however, not been measured during an attack.

### Summary.

Gastric resection was performed on a 51-year-old man owing to duodenal ulcer. Jejunal peptic ulcer soon developed. The symptoms regressed following vagotomy, and roentgen examination showed healing of ulcer. Four months after the operation he committed suicide. Autopsy showed that the ulcer was healed, and there were no signs of regeneration of the vagus nerves.

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## Metal Ions as a Cause of Swelling after Local Anaesthesia in Dental Practice.

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Before the local anaesthetic xylocaine,  $\omega$ -diethyl-amino-2,6-dimethylacetanilid, was launched on the Swedish market at the beginning of the year it had been made the object of comprehensive pharmacological investigations (1) and had been subjected to a series of potency determinations and compared in this respect with procaine (2). It had also been subjected to careful clinical tests for a couple of years. The results, both in surgical (3) and dental (4) practice, were extremely good. No local irritation had been observed. When the preparation had been on the market for some time, it was therefore very surprising to find that in dental practice a local irritation could arise in the form of large doughy swellings, having the same appearance as had earlier been observed after the injection of certain procaine solutions.

As these secondary effects only arose with certain dentists or in certain dental clinics, and then as a rule with a high frequency — in a number of cases almost regularly —, whereas the majority did not obtain any such reactions at all, we considered it probable that the cause was to seek in some circumstance connected with the care and manipulation of the hypodermic syringes, and not with the preparation as such.

After detailed investigations, including chemical, biological and clinical tests, we have come to the conclusion that the formation of edematous swellings is due to the liberation of heavy metals, especially copper, from the metal parts of the syringes, and that this complication may easily be avoided if the syringes

are cleaned, sterilized and kept *lege artis*, and if the solutions to be injected are not unnecessarily exposed in the syringes. This liberation of metal is not something specific for xylocaine-epinephrine solutions. It also takes place with procaine-epinephrine, and is chiefly due to the acid reaction in the solutions, which is necessary for the conservation of the epinephrine. In the following we shall give an account of the experiments carried out and the conclusions at which we have arrived.

## Chemical Investigations.

### A. Spectrographic Analysis.

In two glass hypodermic syringes with metal plungers — one unused, the other used by a dentist whose patients had had edema — “xylocaine-epinephrine 2 %”<sup>1</sup> was allowed to remain for 1, and 2½ hours, after which the original solution and the solutions exposed in the syringes were submitted to qualitative spectrographic analysis. No heavy metals were shown to be present in the original solution, while the solutions from the unused syringe contained copper, nickel and traces of tin, and the solutions from the other syringe contained copper and nickel, in this case more copper than in the solution from the first-mentioned syringe. The quantities of metal increased with the time of exposure in the syringes. — Experiments were also carried out with specially prepared solutions not containing sodium ions — which might conceivably be a disturbing factor in the analysis —, but with the same results. — In our analyses we also looked for other metals, such as aluminium, lead, cobalt, chromium, manganese, molybdenum, platinum, silver, titanium and vanadium; but these were not shown to be present. Zinc was not found in these analyses, owing to the fact that traces of this metal sometimes are difficult to demonstrate spectrographically; but it was, on the other hand, shown in the polarographic analyses, which we shall discuss in the following.

<sup>1</sup> “Xylocaine-epinephrine 2 %” has pH 4 and the following composition:

diethylaminoaceto-2,6-xylidid hydrochloride . . . . .	2.0	gm
epinephrine . . . . .	0.00125	gm (1 : 80,000)
sodium chloride . . . . .	0.6	gm
sodium pyrosulphite . . . . .	0.05	gm
methyl-p-hydroxybenzoate . . . . .	0.1	gm

distilled water to 100 ml

*B. Polarographic Analysis.*

When the spectrographic analyses had shown that certain heavy metals could be liberated, quantitative polarographic determinations were carried out. The solutions were allowed to remain for different periods in syringes of different types — new and used —, after which the content of the liberated metals, viz. copper, nickel and zinc, was determined. The majority of the experiments were performed with the trade-preparation “xylocaine-epinephrine 2 %”, but also a couple of procaine solutions<sup>1</sup> of different composition and solutions not containing any local anaesthetic or sodium chloride were examined. All of these solutions had pH 4. — In order to investigate the importance of the degree of acidity of the solutions, a couple of experiments were carried out with a xylocaine-epinephrine solution of pH 5.5. — The composition of the solutions may be seen from table 1, which also shows the results. The liberated amounts of copper and zinc were, with the xylocaine-epinephrine solution intended for practice, of the same magnitude, or on an average about 0.03 mgm per ml, and greater than the amount of nickel. In one case (no. 7) it was only possible to show the presence of nickel; in another case (no. 5) also cadmium ( $0.01 \text{ mgm} \pm 25 \%$ ) was demonstrated, besides copper, nickel and zinc. The syringes in experiments nos. 1 and 3 had been used by dentists in practice, who had repeatedly observed swellings in their patients after the injections.

The amount of metal liberated from one and the same syringe with one and the same solution may be the same at different times (cf. experiments 1 and 6), but may also be somewhat different (cf. experiments 3 and 4), which is due to the fact that on different occasions the surface of the metal or the alloy may offer different conditions for attack. This makes it difficult to judge the results quantitatively with the different solutions. It would seem, however, that a solution containing procaine instead of

<sup>1</sup> F. i. we used “Injectabile procaini dentale 2 %” according to the prescription published by the Royal Medical Board in the so-called “M. B. 1944”, see table 1, experiment 8. The solution has pH approximately 4 and the following composition:

procaine hydrochloride .....	2	gm	{ (epinephrine 1 : 33,000)
epinephrine solution .....	3	gm	
potassium sulphate .....	0.4	gm	
sodium chloride .....	0.2	gm	
sodium pyrosulphite .....	0.05	gm	
hydrochloric acid (normal).....	0.08	gm	

distilled water to 100 ml

xylocaine — but in other respects having the same constituents and the same pH — liberated metal to about the same extent as the corresponding xylocaine solution. The measurements were carried out at the same time and with xylocaine and procaine alternately (experiments 6 and 9, and 10 and 4 respectively). In the one case somewhat less metal was liberated with procaine than with xylocaine, but in the other the case was reversed. The liberation seems to be mainly due to the acid reaction (cf. experiments 6 and 2 at pH 4 and experiments 14 and 15 at pH 5.5); but the local anaesthetic contained in the solutions (cf. experiment 11), and the sodium chloride present therein (cf. experiments 12 and 13) make the metal parts of the syringes, to judge by all the evidence, more liable to attack.

### Biological Investigations.

In the biological investigations attempts were made to determine the local irritating effect of different metal-containing xylocaine-epinephrine solutions as well as of such solutions without the addition of xylocaine. The method used here has been described by GRÖNBERG (5). According to this method, 0.1 ml of the test-solution is injected between the two dermal layers of the rabbit's ear. White rabbits are most suitable in this connection. The method is extremely sensitive, as it gives response to considerably weaker stimuli than those observable under clinical conditions in man. It is thus not possible to translate these results without further ado to the conditions obtaining for man, but on the other hand such a method has the advantage that it offers the possibility of a direct and quantitative comparison between the irritating effects of solutions that under clinical conditions lie on either side of the threshold of irritation. In order further to increase the sensitiveness of the reaction, we began, after a number of preliminary experiments with the dose recommended by GRÖNBERG, 0.1 ml, to use double this volume, or 0.2 ml.

The macroscopic picture that one obtains, if the injected solution has an irritating effect, consists in a reactive "inflammation" which may manifest itself as a reddening, a swelling (with or without edema), and the appearance of blood-extravasates. Where the effect is stronger, necrosis and in some cases perforation of

the ear may arise. Histologically, one observes first edema, which is then followed by inflammatory cell-infiltration etc.

The local reaction after the injection of a copper containing solution to which had been added epinephrine (0.05 mgm Cu as  $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$  per ml + epinephrine 1:80,000 in physiological salt solution with pH 4) was not very different from that which was obtained after the injection of the trade preparation "xylocaine-epinephrine 2 %" to which had been added copper in the same concentration as in the xylocaine-free solution. It consisted in a reactive "inflammation" manifesting itself above all in a relatively pronounced hyperemia, which was always accompanied by hemorrhages. In addition to this, there was a more or less pronounced edematous swelling. The reaction appeared relatively slowly and remained for a long time. The hemorrhages, especially, required a considerable time for their absorption, on an average about 12 days. Copper-containing solutions of the same concentration as those referred to above but without the addition of epinephrine gave a weaker reaction than those containing epinephrine, probably owing to the fact that in these cases the copper was not retained for an equal length of time at the place of injection.

An addition of nickel (0.05 mgm Ni as  $\text{Ni}(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O}$  per ml) to the epinephrine-containing copper solutions had scarcely any significance. Nickel (0.05 mgm per ml) together with epinephrine or xylocaine-epinephrine did, however, give a certain irritation, manifested in a clear tendency to swellings and hemorrhages. The extent, intensity and duration (on an average 4—5 days) of the reaction were, however, considerably less than in the case of copper. — Zinc (0.05 mgm as  $\text{ZnCl}_2$  per ml) together with epinephrine gave rise like nickel, to, amongst other things, swellings. The duration of the reaction (about 2 days) was considerably shorter than in the case of nickel. It is thus clear that the injurious effects of nickel and zinc are comparatively insignificant in relation to those of copper.

In the histo-pathological examinations of ears into which "xylocaine-epinephrine 2 %" + copper had been injected the picture of a very pronounced, in part hemorrhagic edema together with marked lymphoplasmoleucocytic cell-infiltration was obtained.

If before the experiments the animals were prophylactically treated with 2,3-dithiopropanol (BAL), which, as we know, has

the capacity to bind and thus render innocuous a number of heavy metals, the reaction after the injection of the copper-containing epinephrine solution was weakened. Similar results were obtained by adding thiosulphate to the copper-containing solution.

In these experiments we used the trade preparation "xylocaine-epinephrine 2 %" as a control. It gave a weak and insignificant reaction, which very soon receded. The reaction in this case is probably to be ascribed to the acid character of the solution, as the conserving and epinephrine stabilizing substances in the existing concentrations proved in special experiments to be without any significance. Nor did xylocaine alone in a neutral solution give any reaction.

In this connection it may be mentioned that procaine-epinephrine prepared according to the same formula as xylocaine-epinephrine gave a noticeably stronger reaction than the latter, which manifested itself especially through a high frequency of hemorrhages and the considerably longer time it required for complete healing.

We have only been able to give the main lines of the comprehensive experiments carried out. A more detailed account will be given later (6).

### Clinical Investigations.

In the first experiment 0.04 mgm copper (in the form of the chloride) and 0.01 mgm nickel per ml (in the form of the nitrate) were added to the trade preparation "xylocaine-epinephrine 2 %", which was then injected immediately afterwards — within about 1 hour after the mixing — in 21 healthy persons. The injected volume was 2 ml; the whole amount was administered at once. The injections were made in the left upper jaw between the canine and the first premolar. By way of control, 2 ml of the same solution, but without the addition of the metal salts, was injected at the same time between the same teeth on the right side. Dentists are unanimous in considering swellings to arise especially easily in these regions of the upper jaw.

The results are given in tabular form in table 2. On the left side, where the "poisoned" solution had been injected, greater or lesser swellings arose in all cases; on the other hand, there was not a single swelling. The swelling appeared as a rule after some

hours, in a number of cases not until after the lapse of one day, and it generally remained for 3—5 days. It was always distinctly observable, in several cases very strongly pronounced. In appearance the swellings were soft or doughy; in about half of the cases they were somewhat tender when pressed. It was also of interest to note that the duration of the anaesthesia was in every case shorter than on the control side, which may possibly have been due to an increased rate of inactivation of the epinephrine through the added metals. Such a catalytic effect of certain heavy metals has, of course, been observed before. According to the tests carried out, however, the epinephrine in the solution used by us was not destroyed *in vitro* until after a couple of days.

In the experiments on animals the injury to the tissues was clearly observed also after the injection of only copper-containing solutions. It was, however, necessary to administer epinephrine, which, as we know, delays the resorption, in order to make the reactions more pronounced. In a series of experiments on 10 persons, therefore, the xylocaine and other constituents in the original solution, with the exception of epinephrine and sodium chloride, were excluded. These tests were carried out with a physiological salt solution of pH 4, to which epinephrine in the concentration 1 : 50,000 and 0.05 mgm copper per ml were added. In other respects the method was the same as in the preceding experiments.

The results are given in table 3. Also in this series of experiments, a swelling of the type referred to appeared in all persons. A further reaction in the form of ache, moreover, was noted in all cases, which is not surprising in view of the fact that the solution did not contain any anaesthetic. Where the injection was made in other parts of the body, *e. g.* in the arm, a heavy ache was obtained but no swelling.

In a similar series of experiments on 10 persons, with only zinc to an amount of 0.05 mgm per ml (in the form of the chloride) and with epinephrine and physiological salt solution as in the preceding experiments, the reaction was very slight, only 40 % of the cases reacting with an inconsiderable — scarcely observable — swelling, which quickly receded. Practically all the cases, however, reacted with an ache in the injection-area and with severe headache.

Nickel, which is liberated from the hypodermic syringes in smaller amounts than copper and zinc, was also tested, but in a



lower concentration, or 0.01 mgm per ml (administered in the form of the nitrate). The number of persons and the experimental conditions were in other respects the same as in the tests with the other metal ions. None of the cases showed any swelling after the injection of the nickel-containing solution. With higher concentrations it would doubtless have been possible to produce a certain degree of swelling also with nickel — the experiments on animals indicate as much —, but as larger amounts of nickel do not occur in actual practice we considered further experiments superfluous in this connection.

In further experiments with metal-containing solutions the conditions obtaining in practice were produced by retaining the injection-solutions in the syringes for a longer or shorter period before the injection. Two solutions were used in the experiments, namely "xylocaine-epinephrine 2 %", and the previously mentioned procaine-epinephrine solution according to "M. B. 1944" (see note on p. 241) — both with pH about 4. In the one series we used a new all-metal syringe of Swedish manufacture (no. 3 in table 1), and in the other an original Fischer syringe. The injections were made on the one side of the upper jaw at the canine or one of the premolars; the controls, with solution taken direct from the packing, at the corresponding place in the other half of the jaw. 2 ml was injected each time. The swellings which arose were of exactly the same appearance as in the preceding experiments. The time for the occurrence of the reaction and its duration were also as before. In no case was there any swelling on the side where the control solution had been injected.

From table 4, which shows the results with the all metal syringe, it appears that even after such a short period of exposure as 10—15 min. sufficient metal has been liberated to give rise to an irritation. For the rest, it is not necessary for the syringe to be filled with solution during the exposure. It is sufficient if traces of the solution are left, and then mixed with fresh solution. Even such small amounts as may remain from an earlier injection are enough. This will be readily understood if one bears in mind that only a slight amount of solution, or a "fluid film", is needed to cover the surface of metal from which the liberation takes place. — All this obviously applies to both the xylocaine and the procaine solutions, between which there were no definite differences.

In the experiments with the other syringe the results were a good deal more favourable. From table 5 we see that as long as

the syringe was new and in good condition, it was not possible to produce any swellings with the xylocaine solution, even after such a long period of exposure as 2 hours. When the nickel plating on the plunger and the metal end-piece had been artificially impaired — in order to reproduce the conditions in a much used instrument —, swellings appeared with both the solutions, though only after an exposure of 45—60 minutes. This syringe was thus of considerably better quality than the all-metal syringe used, which we would designate as unusable in dental practice.

The results attained are also confirmed by a number of other observations, one of which especially deserves to be mentioned. — At a clinic with a high frequency of side actions it had been customary to fill several syringes at once in order to save time (among these syringes was also no. 1 in table 1); these were then used in the course of the day. The syringes were, moreover, cleaned and boiled only once a day. If it proved necessary to use a syringe several times, only the needle was changed. After the technique had been rectified in these points, 10 of the previously treated patients were called in at our request for renewed injections. All of them had previously always reacted with swellings, as a rule several times — in one case as many as four times — in succession. — In no case were any local reactions now obtained, not have there been any such at this clinic in the sequel.

It might be remarked that the volume of the injected solution might play some rôle in the appearance of the swellings. The possibilities of absorption of larger volumes of liquid might seem limited in the areas here in question, especially if the solutions contain epinephrine. For infiltration anaesthesia with the 2 % solution 1—1.5 ml is a sufficient amount. In 20 cases, however, we injected 3—4 ml at once and in the same place without any side actions.

### Discussion.

We have shown experimentally that acid solutions of the local anaesthetics xylocaine and procaine may liberate metals — copper, nickel and zinc — from the hypodermic syringes, and that such metal-containing solutions give rise in the rabbit's ear — which is an extremely sensitive test-object — to tissue-injuries, especially serious with solutions containing copper ions. The injection of such solutions in the jaws gives rise after some hours to

characteristic local reactions in the form of swellings which remain for several days. These are of precisely the same type as those observed in dental practice. Of the metal ions studied, especially copper has proved apt to produce the swellings, but also zinc — though only in a slight degree — may produce the same secondary effect. In the concentration in which it may occur in practice, nickel does not give rise to swellings. From our experiments it would seem that the reaction is mainly due to a direct toxic effect of the liberated metals. That in minimal concentrations copper may have toxic effects — so-called oligo-dynamic action — on certain lower plants has been known since VON NÄGELI's (7) investigations; and the observation has been confirmed on other and higher organisms by, inter alia, NAUMANN (8). A toxic effect has also been clearly observed in tissue cultures (9). We have not, however, found any description of effects resembling that studied here in the literature. It is not out of the question that also other factors besides the toxicity of metals may play a certain rôle, for example, conversion products of the epinephrine, to which an injurious effect may possibly be due (inactivation of the epinephrine is catalyzed by the metal ions). Xylocaine as such, sodium pyrosulphite and the disinfecting agent methyl parahydroxybenzoate — in the concentrations in which they occur in the trade preparation — are not the cause of the swellings, nor is the xylocaine-epinephrine solution in its entirety.

That procaine may give rise to swellings is nothing new for those engaged in dental practice. In the Swedish literature there are also a couple of works dealing with this problem (10, 11). BRYNOLF (10) used five solutions of different composition, and got swellings of the same type as that described here with all the solutions except one. This author also discussed the significance of the addition of pyrosulphite. One of the solutions used, prepared according to a recipe by RINGSTRÖM (12), did not contain sulphite, but also this solution gave rise to side actions. RINGSTRÖM himself, however, did not obtain any swelling from this solution (13). The solution that in BRYNOLF's practice did not give rise to a swelling had pH about 5.5, while the other solutions, including RINGSTRÖM's had pH about 4, according to our control. BRYNOLF considered that the degree of acidity might be of a certain significance, but she presumably overlooked the fact that "novocaine-corbasil" in cartridges, which did not give any local reactions, had pH about 4. Another interesting observation is the fact that the

anaesthesia was better with the solution that did not give rise to any side actions, than with the other solutions. This, of course, is precisely in agreement with our observation of a less satisfactory anaesthesia with the metal containing solution. The hydrogen-ion concentration in unbuffered solutions, on the other hand, plays no rôle for the time of onset of the anaesthesia or its duration, according to recent investigations (2, 14). We do not, it is true, know what syringes were used in BRYNOLF's investigations, but everything indicates that in this case, too, it was a question of a metal effect. Also concerning the other investigation mentioned (11), dealing with the cause of swellings after the use of an acid (pH about 4) procaine solution in military dental clinics, there is nothing to contradict our interpretation.

It is clear that swellings and other local irritation may be conceived to arise also from other causes than metal effect, *e. g.* in poor nutritive and circulatory conditions, in connection with inflammatory processes, with oversensitiveness to one or another constituent in the solutions, with the use of unsterile solutions and syringes, with the use of an unsuitable preserving liquid, after mechanical tissue-injuries and so forth.

We consider, however, that the main cause of the swellings after the use of xylocaine has been explained adequately by the experiments we have carried out. Even if the actual mechanism for the effect of the metals is unknown, it has in these cases nevertheless been the liberated metals, chiefly copper, that have given rise to the complications. In practically all the cases of swelling after xylocaine that we have had the opportunity of investigating — we have not had occasion to deal to the same extent with the complications with procaine —, it has been possible to trace the cause to a metallic impurity; and after elimination of the source of the trouble the swellings have not appeared. The majority of dentists, however, have not observed any swellings in their patients, which must be considered to be due to their care of their syringes. A good example of this is provided by the dental treatment of school-children in Gothenburg by a group of 36 dentists, who have performed about 8,000 injections without a single case of swelling (15).

How then, should the hypodermic syringes be cared for in order to avoid the complications referred to? When one knows the cause, the procedure becomes obvious. One must not, as in some clinics, allow the solution to remain for a longer period in the

syringes, and one must not leave any traces in the syringes or the needles between the injections, for even small amounts of fluid may cause the metal parts of the instrument to be attacked. If the syringes are rinsed with alcohol or some other such agent then used fluid must not be squirted back into the container with syringes. One must not dry-sterilize syringes or needles without previously cleaning them, and one must of course not squirt back solution that has not been used into the vial once it has been taken into the syringe, which has also occurred. Instead, the solution should not be taken into the syringe until just before it is ready to be used. This does not mean that one need be in any way hurried. If the syringe is of good quality, one can, as our experiments and our experience show, take plenty of time. When the injection has been given, if one wants to keep one's syringes in good condition, one should draw up a little water several times, so that the needle and also the nozzle are roughly rinsed. If one takes this little bit of trouble, the more careful cleaning may be postponed until a suitable occasion; otherwise, it should be done as soon as possible after use, to avoid corrosion. For the more thorough cleaning one should first squirt all the solution out of the instrument — if this has not already been done —, after which the syringe is taken to pieces. Each part is then rinsed separately, before sterilization by boiling takes place. After the sterilization the syringe may be put in preserving fluid if this is used. It is preferable to use a special vessel for boiling the syringes, and not to mix them with other instruments. The water in this vessel should of course be changed each time. As regards injection-syringes, those made entirely of glass are to be preferred, and in this case the above procedure for cleaning can be considerably simplified. Fischer and record syringes are also good, but they should be of good quality. All-metal syringes, on the other hand, should not be used.

### Summary.

Thorough chemical, biological and clinical tests have been carried out to ascertain the cause of the swellings sometimes occurring in dental practice after the injection of local anaesthetics.

In the chemical investigations, including spectrographic and polarographic analyses, it is shown that acid solutions of xylocaine

and procaine liberate in certain circumstances small amounts of copper, nickel and zinc from hypodermic syringes made entirely or partly of metal.

According to the biological determinations carried out upon an extremely sensitive test-object — the ear of rabbit —, solutions containing these metal ions give rise to tissue-injuries. These are especially pronounced after the injection of solutions containing copper, but are comparatively insignificant after nickel and zinc.

In the clinical experiments it is shown that copper-containing solutions with or without anaesthetic, and acid solutions of xylocaine and procaine that have for a certain time been exposed in the syringes before the injections give rise to swellings of the same type as those observed in dental practice. They appear after some hours and remain for several days. In the concentrations in which according to the chemical analyses these metals may occur, zinc and nickel cause slight or no injury.

The results obtained are discussed, and practical instructions are given to avoid this complication.

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Table 1.

*Polarographic Determinations of the Amount of Metal Obtained from Different Hypodermic Syringes with the Use of Different Solutions.*

Experi- ment	Solution used	Type of syringe	Time of exposure in hours	Amount of metal obtained in mgm per ml solution		
				Cu	Ni	Zn
1	"Xylocaine-epinephrine 2 %" in the form of trade preparation (pH 4)	Fischer syringe; American manufacture. Used.	2	0.04 ± 10 %	0.005 ± 50 %	0.04 ± 10 %
2	— » —	Fischer syringe; Swedish manufacture. Not used before.	2	0.01 ± 25 %	0.005 ± 50 %	0.01 ± 25 %
3	— » —	All-metal syringe (chromo- plated); Swedish manu- facture. Slightly used (for the exper- iments in table 4).	0.5	0.03 ± 10 %	—	0.03 ± 10 %
4	— » —	— » —	0.5	0.07 ± 5 %	0.005 ± 50 %	0.02 ± 15 %
5	— » —	Record syringe; English make. Used.	0.5	0.01 ± 25 %	< 0.001	0.02 ± 15 %
6	— » —	Same as in experiment 1.	2	0.04 ± 10 %	0.005 ± 50 %	0.03 ± 10 %

7	— » —	Record syringe; Swedish manufacture. Not used before.	2	—	< 0.002	—
8	Procaine-epinephrine according to "M.B. 1944" (pH 4).	Same as in experiments 1 and 6.	2	0.01 ± 25 %	0.005 ± 50 %	0.02 ± 15 %
9	Procaine-epinephrine prepared according to the Xylocaine-epinephrine formula (pH 4).	Same as in experiments 1, 6 and 8.	2	0.02 ± 15 %	0.005 ± 50 %	0.03 ± 10 %
10	— » —	Same as in experiments 3 and 4.	0.5	0.13 ± 5 %	0.005 ± 50 %	0.07 ± 5 %
11	Prepared according to the Xylocaine-epinephrine formula but without any local anaesthetic (pH 4).	Same as in experiments 1, 6, 8 and 9.	2	0.01 ± 25 %	< 0.001	0.03 ± 10 %
12	Prepared according to the Xylocaine-epinephrine formula but without any sodium chloride.	Same as in experiments 1, 6, 8, 9 and 11.	2	0.01 ± 25 %	< 0.002	0.02 ± 15 %
13	— » —	Same as in experiment 2.	2	—	< 0.002	0.01 ± 25 %
14	Prepared according to the Xylocaine-epinephrine formula but with a higher pH-value (5.5).	Same as in experiments 1, 6, 8, 9, 11 and 12	2	0.02 ± 15 %	0.004 ± 50 %	0.03 ± 10 %
15	— » —	Same as in experiments 2 and 13.	2	< 0.001	0.004 ± 50 %	0.01 ± 25 %



Table 2.

*Results after Injection of 2 ml "Xylocaine-Epinephrine 2 %" to which has been added 0.04 mgm Cu++ and 0.01 mgm Ni++ per ml (21 persons aged 23-45 years, nos. 1-17 ♂, nos. 18-21 ♀).*

Experi- ment	Degree of swelling + = moderate swelling ++ = strong swelling	No. of hours after the in- jection for appearance of swelling	Duration of swellings in days	Remarks
1	+(+)	3	2½	During first hours after appearance of swelling aching sensation in left cheek. 2nd day swelling somewhat reduced; cheek tender when pressed.
2	+	13	2	Smarting ache in left cheek 4-5 hours after the injection. Cheek tender when pressed for about 4 days.
3	+	Appeared during night after about 9 hours	4	—
4	++	2	5	After 24 hours swelling larger and more sagging. Left cheek tender. Slight headache.
5	++	3	5	Swelling increased after 24 hours. Sank during 2nd—3rd day.
6	+(+)	1½	7	During first hours after appearance of swelling ache in left cheek. Tenderness persisting for 3 days.

7	+	$1\frac{1}{2}$	$2\frac{1}{2}$	Left cheek tender when pressed.
8	++	1	$2\frac{1}{2}$	—
9	+	5	3	—
10	+	12	4	Somewhat tender during first 24 hours.
11	+	5	$3\frac{1}{2}$	Left cheek tender when pressed.
12	+	$5\frac{1}{2}$	$1\frac{1}{2}$	—
13	+	$\frac{1}{2}$	$5\frac{1}{2}$	20 min. after injection pricking sensation in left cheek; stopped after about $1\frac{1}{2}$ hrs.
14	++	Was not observed until following day	3	—
15	++	$\frac{1}{2}$	4	Left cheek tender when pressed.
16	+(+)	$\frac{1}{2}$	$4\frac{1}{2}$	—
17	+	1	4	—
18	+	Following day	4	Left cheek tender.
19	+	1	4	Left cheek tender.
20	++	Immediately	$4\frac{1}{2}$	—
21	++	1	4	—

Table 3.

Results after the Injection of 2 ml Physiological Salt Solution to which had been added 0.05 mgm  $\text{Cu}^{++}$  per ml and Epinephrine to Conc. of 1:50,000 (10 persons aged 25—40 years, nos. 22—30 ♂, no. 31 ♀).

Experi- ment	Degree of swelling. + = moderate swelling ++ = strong swelling	No. of hrs. after the in- jection for appearance of swelling	Duration of swelling in days	Remarks
22	+	Immediately	3½	After about 10 min. heavy ache for ½ hour.
23	++	¾	7	Ache for 1 hr. Swelling increased after 2 days.
24	+	½	7	Ache for 10 min. Swelling increased during 2nd day.
25	++	3	4	Ache for 5 min. Swelling increased after 2 days.
26	+	4	4	Heavy ache after about 1 hr., lasting for couple of hrs.
27	+	2	7	Smarting pain for 5 min.
28	++	Immediately	8	Ache for about ½ hr. After 2 days increased swelling. Gum tender.
29	+	1½	3	Ache for 2 hrs.
30	++	Immediately	7	Heavy ache for 10 min.
31	++	1	9	Heavy ache for 1 hr. Increased swelling after 24 hours.

Table 4.

*Results after the Injection of 2 ml "Xylocaine-Epinephrine 2 %" and 2 ml Procaine-Epinephrine Respectively, which had been exposed in a New (unused) All-metal Hypodermic Syringe (no. 3 in table 1) for Different Periods before the Injection.*

Experi- ment	Time of exposure	Degree of swelling 0 = no swelling + = moderate swelling ++ = strong swelling
<i>A. "Xylocaine-epinephrine 2 %"</i>		
52	10 min.	+
53	15 min.	++
54	15 min.	0
55	35 min.	+
56	45 min.	++
57	45 min.	+
58	70 min.	+(+)
59	80 min.	+
60	145 min.	++
61	2 hrs. with traces from a previous filling, thereafter 3 min. with fresh solution.	+
<i>B. Procaine-epinephrine according to "M. B. 1944"</i>		
62	15 min.	+
63	15 min.	+
64	20 min.	+(+)
65	25 min.	++
66	30 min.	++
67	30 min.	++
68	40 min.	+(+)
69	45 min. with traces from a previous filling, thereafter immediate injection of fresh solution.	+(+)

Table 5.

*Results after the Injection of 2 ml "Xylocaine-Epinephrine 2 %" and Procaine-Epinephrine Respectively, which had been exposed in a Fischer Hypodermic Syringe for Different Periods before the Injection. (The Syringe had not Previously been used. Before Experiment no. 78 the Syringe was Intentionally Impaired; the Experiments nos. 78—88 were performed after this Change.)*

Experi- ment	Time of exposure	Degree of swelling 0 = no swelling + = moderate swelling ++ = strong swelling
<i>A. "Xylocaine-epinephrine 2 %"</i>		
70	5 min.	0
71	40 min.	0
72	45 min.	(+)
73	60 min.	0
74	60 min.	0
75	70 min.	0
76	130 min.	0
77	4 hrs. with traces from a previous filling, thereafter 5 min. with fresh solution.	0
78	25 min.	0
79	60 min.	(+)
80	60 min.	+
81	60 min.	++
<i>B. Procaine-epinephrine according to "M. B. 1944"</i>		
82	20 min.	0
83	30 min.	0
84	45 min.	+
85	45 min.	0
86	50 min.	0
87	50 min.	+
88	60 min.	+

From the Coastal Hospital at Refsnæs, Denmark.  
(Senior Surgeon: JOHANNES MEYER, M. D.)

## On the Formation of Calculi in the Urinary Tract of Patients with Osteo-articular Tuberculosis.<sup>1</sup>

By

JOHANNES MEYER and ELSE MOGENSEN.

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The calculi in the urinary tract which we are going to deal with today are stones formed in *non-infected urine*. If an *exact* distinction between these stones and such as are formed in urine infected with urea-splitting bacteria is not made in a work dealing with the pathogenesis and treatment of calculi in the urinary tract, then false conclusions will be arrived at.

In spite of numerous endeavours we have, as yet, not managed to elucidate the pathogenesis of calculi formed in non-infected urine — the formation of the so-called *primary calculi*.

One school of investigators have held the view that the cause of the stones had to be sought in disturbances of the content of *colloidal* substances in the urine. Another school believed to find the cause in changes of the content of *crystalloid* constituents in the urine — such as calcium, phosphorus, oxalic acid etc. Lastly, the American RANDALL<sup>2</sup> has more recently drawn attention to the frequency of small calcified plaques in and upon the renal papillae, and believes thus to have found the first stage of the calculi in the urinary tract. In contrast with the two other schools mentioned above, RANDALL need not reckon with changes in the composition of the urine as contributing to the occurrence of the stones, since the plaques grow — at first fixed on the renal pa-

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<sup>1</sup> Read before the Danish Society of Surgeons.

<sup>2</sup> RANDALL: VII Congress of the International Society of Urology, New York 1939.

pillae, later freely in the renal pelvis — exclusively by means of precipitations from the quite normal urine.

This is just the attractive part of RANDALL's theory, as an important reason why we have been unable to agree upon the pathogenesis of the calculi in the urinary tract just is that, generally, it has been impossible to demonstrate any change whatever in the composition of the urine of patients with primary calculus-formation in the urinary tract, in spite of the fact that such stones are constantly added to by fresh layers.

What are then the conditions of the precipitation of the calculus-producing substances from such quite normal, clear urine?

The question may be briefly answered as follows:

When urine is considered a simple aqueous solution of different salts, *a careful computation shows that normal urine is moderately supersaturated with regard to the salts present in the concretions in the urinary tract: The supersaturation is not so great but that it is fully comprehensible that normal urine may remain completely clear without any sediments for a long time. On the other hand, the supersaturated condition of the urine explains without any difficulty that a concretion may grow in quite normal urine — the calculus acting as a crystallization centre in a supersaturated solution.*

But this fact that calculi in the urinary tract may grow, and generally do so, in a completely normal urine, must necessarily lead to the conclusion that the actual pathological phenomenon of the genesis of concretions in the urinary tract is the *formation of the stone nucleus and the retention* of the small new-formed stone nucleus in the urinary tract. The further development of the stone nucleus takes place under quite normal conditions in urine and in the urinary tract.

The essential problem in the pathogenesis of these calculi will then be: *How does the formation of the stone nucleus take place?*

RANDALL's theory *may* be correct but is very difficult to prove, at any rate clinically, as the first stages of the calculus-formation will then evade observation. In 1927<sup>1</sup> we dealt with the problem of the pathogenesis of the primary calculus-formation and made — as a mere hypothesis — the supposition that the formation of the stone nucleus took place as a consequence of *transient changes in the content of crystalloid constituents in the urine*, with a resulting vigorous and dense sediment-formation,

<sup>1</sup> JOHANNES MEYER: Z. f. klin. Medizin 111, 613, 1929.

and *under conditions favouring a retention* of minute lumps of crystals in the urinary tract.

It is obvious now that if an attempt has to be made to clear up the cause — or causes — of stone nucleus-formation by means of clinical examinations, we must concentrate our investigations on the urine and the state of the urinary tract in *patients who, clinically, display the picture of a constant formation of stone nuclei* — i. e. patients who during *repeated* attacks of ureteral colic *constantly* pass small concretions and lumps of crystals.

Such patients are not numerous — in particular they are only rarely met with in hospital, and that for a short period. Only special circumstances cause such patients to be seen in hospital in any great number and for a longer period, when a closer examination will be possible.

In the following we shall account for a series of examinations we have succeeded in performing on *a group of such patients*.

In the course of the years 1928 to 1939 a number of 34 adult patients in the "Kysthospitalet paa Refsnæs" displayed signs of concretions in the urinary tract. In practically all the cases the calculous affection manifested itself by *repeated typical attacks of ureteral colic*, most frequently followed by the *discharge of small calculi*.

As a rule, all symptoms of the presence of calculi then disappeared. Only in a small number of cases — a total of 5 patients — *larger calculi* had to be removed later on by operation.

The distribution of stones in the different categories of patients in the coastal hospital will appear from Table I:

Table I.

*Occurrence of Urinary Calculi in Adult Patients Treated at the Coastal Hospital, Refsnæs, 1928/30.*

	Total	Patients with calculi in urinary tract	
		Number	%
<i>Patients with extrapulmonal tuberculosis<sup>1</sup> ..</i>	748	34	4.5 %
<i>Patients with tuberculosis<sup>1</sup> in joints and bones</i>	312	34	10.9 %
<i>Patients with tuberculosis<sup>1</sup> in the vertebral column, the pelvic bones, hip- and knee-joint</i>	176	34	19.4 %

<sup>1</sup> Including a small number of patients with non-tuberculous disorders.



It will be seen that the 34 patients suffering from calculi constitute 4.5 per cent. of all the patients treated in the coast hospital.

It will moreover appear that all the 34 patients suffering from calculi were to be found among patients with processes in joints and bones — but among the considerable number of patients with tuberculosis of the soft parts, signs of calculi in the urinary tract were never observed. Further, it appeared that the calculi only occurred in patients with processes in *the vertebral column, the pelvis and the big joints of the lower extremities*. In about 20 per cent. of the cases these localizations were complicated with calculi in the urinary tract, while they never occurred in case of other localization of osteo-articular tuberculosis. In 3 per cent. of the cases the stones were so large that they had to be removed by operation later on.

The whole of this picture corresponds well to what has been communicated from other hospitals — *e. g.* by PAUS from the Martina Hansen's Hospital near Oslo,<sup>1</sup> by KEY<sup>2</sup> *et al.*

Is it possible in these patients suffering from calculi — possibly in other patients with the said localizations of osteo-articular tuberculosis — to demonstrate deviations from the normal as far as urinary tract and urine are concerned, deviations which can account for the production of stone nuclei that is going on?

First, the *urinary tract*:

All the said patients who were suffering from calculi have been submitted to *confinement to bed of long duration* — many of them exclusively in the dorsal position. Treatment with confinement to bed averages about one year in the 34 patients before the symptoms of the presence of calculi appeared. This particular posture of the urinary tract must, of course, materially favour a retention of possible precipitations in the urine — and the formation of the precipitations as well. It should, however, be noted that *many cases of tuberculosis of the soft parts* have also been treated with confinement to bed of long duration. Thus, in the course of the years 1937 to 1945, a total of 31 cases of tuberculous salpingitis and peritonitis were treated with confinement to bed averaging 11 months, without developing any calculi. Still, the immobilization in the dorsal posture was undoubtedly more absolute in patients with spondylitis and coxitis than in those suffering from tuberculosis of the soft parts.

<sup>1</sup> Norsk Magasin f. lægevidenskab 3, 2260, 1939.

<sup>2</sup> British Medical Journ. I, 1150, 1936.

In 9 of the patients with calculi we could moreover ascertain the presence of *local processes* — abscesses of the psoas and the like — which may have favoured the retention of precipitations in the urinary tract. It must, however, be added that the percentage of such local processes was still greater in patients with tuberculosis of the soft parts — *e. g.* in cases of salpingitis and peritonitis — who, as a rule, had large firm swellings and infiltrates in the pelvis minor.

There can thus be no doubt that the possibilities of retention of small sediments in the urinary tract were far greater in the patients with calculi than in normal persons out of bed, whereas such difference could not be demonstrated with certainty between the patients with calculi and those with severe tuberculosis of the soft parts who did not develop any calculi.

But how about *changes in the composition of the urine*?

In measuring a number of about 1,400 urines of the 24 hours it appeared that the *diuresis* of *patients* — with osteo-articular tuberculosis and with affections of the soft parts (both in bed and out of bed) — on an average was lower by about 14 per cent. than that of normal persons out of bed. The diuresis of patients suffering from *calculi* was not lower than that of patients of the remaining categories. Such decrease of the diuresis will presumably be tantamount to a general increase of all the concentrations of the urine — still, not so great as one might be inclined to believe. For the concentrations of the urine are not inversely proportional to the diuresis, as the quantities in grammes in the 24 hours decrease and increase with the diuresis. The *cause* of the reduced diuresis that has been ascertained is presumably the intense evaporation of water from the surface of the body produced by an energetic sun-, light- and open air-treatment.

In examinations of the diuresis a difference was thus also ascertained between patients and normal persons — but not between patients with and without calculi.

The next question is whether there were other changes in the concentration of the urine which might be in causal relationship to the formation of stone nuclei.

Forty-eight of the small *concretions* passed by the patients were analysed by means of roentgen spectrography. It appeared that primarily they all contained calcium oxalate — either as sole constituent or combined with smaller proportions of calcium phosphate. Calcium was thus a constituent common to the pre-

precipitated substances and, consequently, an examination of the calcium concentration of the urine had to be the main object of a closer analysis of the urines of our patients. In addition, an examination of the phosphoric and oxalic acid concentrations and of the hydrogen ion concentration might be of interest when estimating possibilities of precipitation of the substances found in the calculi.

An examination of these concentrations in *patients with and without calculi* did not, however, show any safe difference between the two groups of patients, but in the course of our considerations of this discouraging result an important fact was, however, realized:

In practically all cases the symptoms of calculi appeared in the course of, or in direct connection with, *the periods of the osseous affection when progressive decomposition of the bone could be observed in the X-ray* — or, in other words, in connection with the so-called “active” stage of the affection of the bone.

The supposition then suggested itself that, somehow or other, there was a causal relation between this well-defined period in the course of the disease and the calculus-formation. If so, an examination of the urine concentrations *just during that period* might possibly afford interesting information when the results were compared with those of similar examinations made during other periods of the disease and in patients without any affection of the bone.

The reason why the examinations of the urine of patients suffering from calculi had not afforded any information of interest was presumably that the analyses had often been made at an advanced stage — long after the ureteral colic had ceased.

Therefore the urine was now examined in a great number of patients with osteo-articular tuberculosis — whether they were suffering from calculi in the urinary tract or not — and the results of analysis arrived at were then considered in relation to the active and inactive periods of the affections of the bones, such as they appeared from long series of X-rays clearly showing the course of the disorder of the bone. In addition the urine was examined in a number of patients with tuberculosis of the soft parts.

We shall now show you the results of our examinations (Fig. I).

This shows the maximum concentrations of calcium in a number of  $3 \times 24$  hours' urines of normal persons and of different

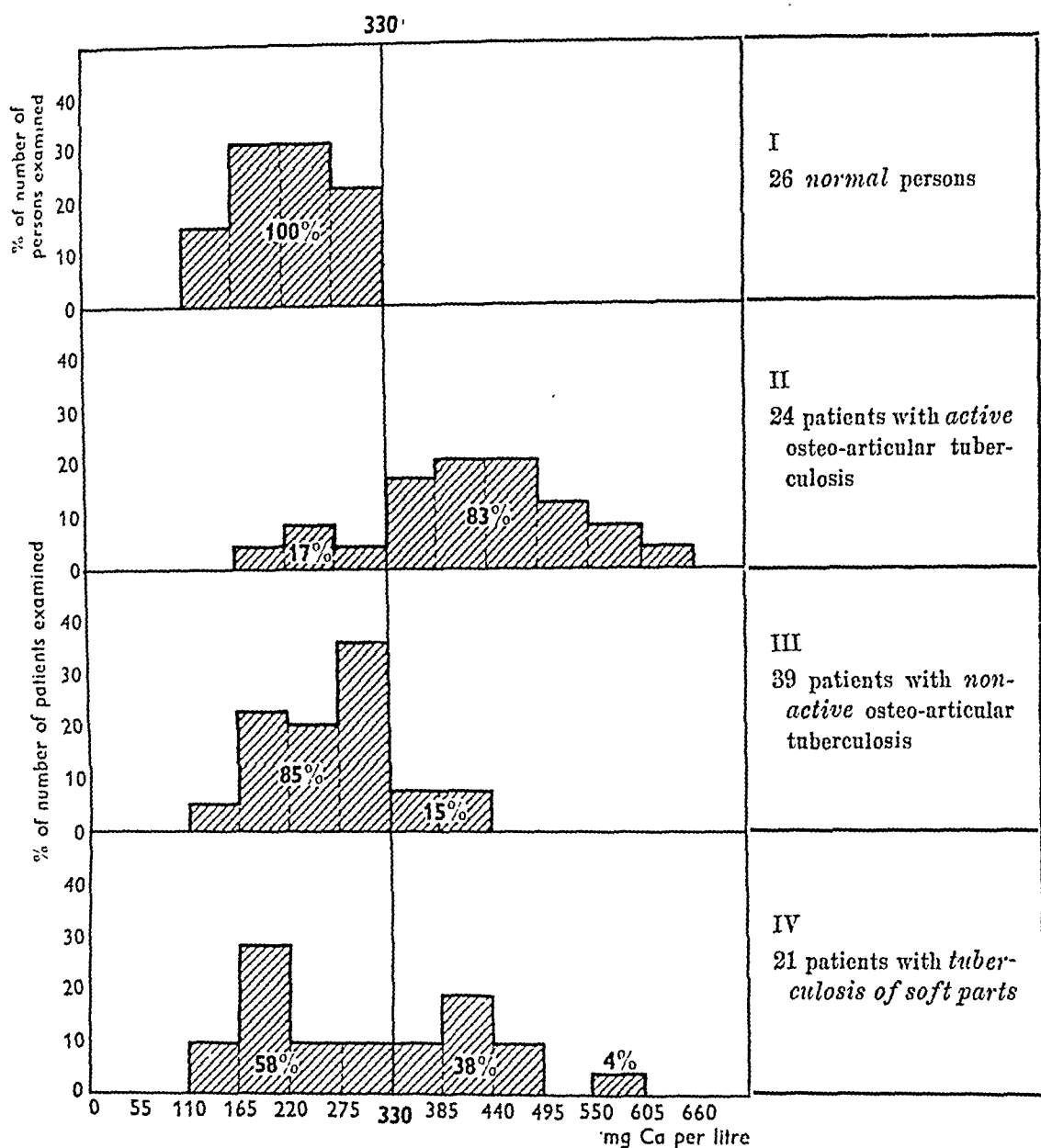


Fig. I. Maximum concentrations of calcium in  $3 \times 24$  hours' urine.

The four hatched areas (I, II, III and IV) are composed of a series of co-ordinated rectangles the base of which corresponds to a definite concentration interval on the absciss, and the height of which states the percentages of the patients in the group whose maximum calcium concentration in  $3 \times 24$  hours' urine is within the interval stated on the absciss.

The four hatched areas become equally large, as they all represent 100 per cent. of the patients in the group in question.

The figures stated in per cent. represent the fraction of the area that is under or over 330 mg. Ca per litre — i. e. the fraction of the patients in the group that has maximum calcium concentrations of more or less than 330 mg. Ca per litre in  $3 \times 24$  hours' urines.

groups of patients (all the persons examined had an ordinary mixed diet). It will be seen that in *normal persons* the maximum calcium concentration never exceeds 330 mg. per litre. This is in complete conformity with similar examinations communicated in the literature. LERICHE<sup>1</sup> has thus pointed out that in the urine of normal persons the calcium concentration fluctuates within rather narrow limits — irrespective of the calcium content of the diet. No doubt, it can be properly maintained that the normal calcium concentration only in extremely rare cases will exceed about 330 mg. per litre.

If we then include *all* urines of the 24 hours in the statement (and not only those with maximum calcium concentrations), reckoning with the *number of urines of the 24 hours* instead of the *number of patients*, then the picture is the same in principle (Fig. II).

None of the urines of the 24 hours of *normal persons* contain more than 330 mg. calcium per litre — whereas 55 per cent. of urines of the 24 hours collected during *active periods* of osteo-articular tuberculosis contain more than 330 mg. calcium per litre. In the course of *inactive periods* the concentration approaches the one found in normal persons, while the cases of *tuberculosis of the soft parts* with regard to the calcium concentration in the urine are still somewhere between the two groups of osteo-articular tuberculosis — however, nearest to the cases of active osteo-articular tuberculosis.

The picture of the variation of the calcium concentration becomes most perfect when the figures are arranged, not only in relation to the different groups of the disease, but *also in relation to the course and treatment with confinement to bed* within the different groups of the disease.

Table II is such an arrangement of the figures. As already mentioned, it has considerable advantages but also the drawback that the number of urines of the 24 hours forming the basis of computation for the individual figure becomes far smaller — and this is seen in several figures of the table.

Here, as in the other tables, it will be seen that no urine of the *normal persons out of bed* contains more than 330 mg. calcium per litre.

In patients with *active tuberculous processes in joints and bones* no less than *74 per cent.* of the urines of the 24 hours contained more than 330 mg. calcium per litre during the first 6 months

<sup>1</sup> R. LERICHE: *Physiol. et pathol. du tissu osseux*, Paris 1939, p. 359.

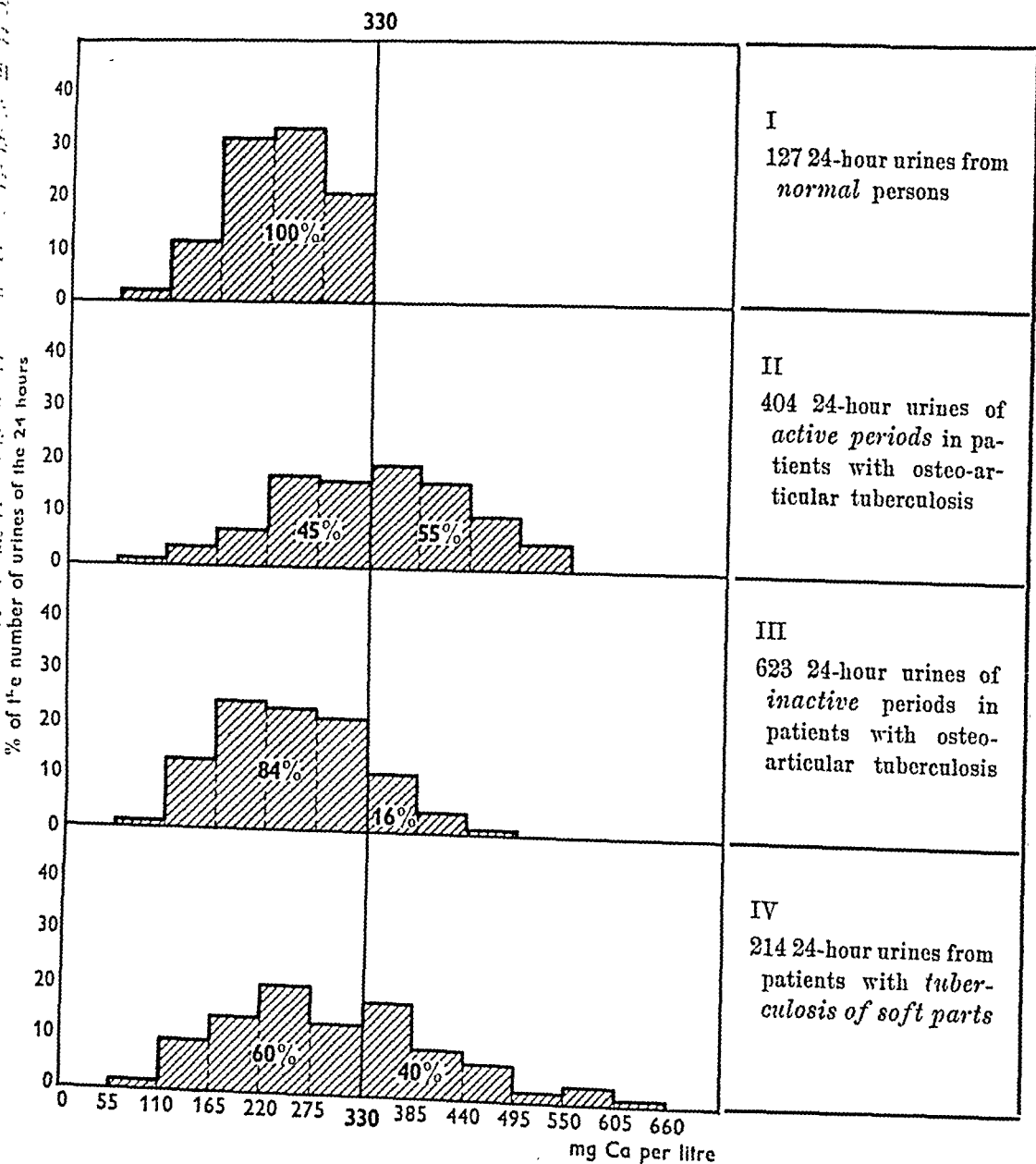


Fig. II. Calcium concentrations in 24 hours' urine.

The four hatched areas (I, II, III and IV) are composed of a series of co-ordinated rectangles the base of which corresponds to a definite concentration interval on the absciss, and the height of which states the percentage of the 24 hours' urine in the group in which the calcium concentration is within the interval stated on the absciss.

The four hatched areas become equally large, as they all represent 100 per cent. of the 24 hours' urines of the group in question.

The figures stated in per cent. represent the fraction of the area that is under or over 330 mg. Ca per litre — *i. e.* the fraction of 24 hours' urine of the group which contains more or less than 330 mg. Ca per litre.

Table II.

*Table of Calcium Concentrations in 24 Hours' Urines of Patients in Bed or out of Bed, and in Normal Persons.*

	Total number of 24 hours' urines	Confined to bed						Out of bed	
		Number of 24 hours' urines analysed	% of 24 hours' urines analysed with calcium concentration exceeding 330 mg. per litre  during confinement to bed for				Number of 24 hours' urines analysed	% of 24 hours' urines analysed with calcium concentra- tion exceeding 330 mg. per litre	
			1st half year	2nd half year	3rd half year	4th half year			
Normal persons.....	127							127	0 %
Patients with osteo- artic. tuberculosis									
active periods .....	404	404	74 %	57 %	40 %	4 %			
inactive periods....	623	392	30 %	20 %	29 %	20 %	327	6.1 %	
Patients with tubercu- losis of soft parts....	214	117	55 %	47 %	0 %	0 %	97	38 %	

of confinement to bed when the process generally displays its greatest activity. Gradually, with decreasing activity — the patients still being confined to bed — the number of high calcium concentrations becomes as low as 4 per cent. during the fourth half-year of confinement to bed. However, the reason why this figure is so low is presumably a mere accident because of the small number of urines of the 24 hours — 26 in all — used in the computation of this figure.

In patients with *inactive tuberculous affections of bones and joints* the number of high calcium values is fairly constant during the confinement to bed — being about 20 to 30 per cent. The initial rise observed in the cases of active tuberculosis is not seen. When these patients come out of bed, the number of high calcium concentrations falls to 6 per cent.

Before considering the figures relating to *tuberculosis of the soft parts* we would premise that it is more difficult to estimate these figures than the preceding ones. First, it has not been attempted to divide the cases of tuberculosis of the soft parts into active and inactive processes, as we have no sufficiently reliable objective criterion by which to do so. The great majority of the patients confined to bed with tuberculosis of the soft parts undoubtedly

have active processes — but some of the cases of active tuberculosis of the soft parts also occur among the patients who are not treated with confinement to bed. Secondly, the number of urines of the 24 hours on which the computation of the individual figures is based is considerable smaller in this group than in the other groups, which causes the figures to be doubtful.

On looking at the figures in the table, it will appear that in patients with tuberculosis of the soft parts the number of high calcium concentrations is not so great during the first half-year of confinement to bed as in cases of active osteo-articular tuberculosis. This might, of course, be due to the fact that inactive, slightly toxic processes are hiding among the cases of tuberculosis of the soft parts confined to bed. But, no doubt, the number of such processes is not so great as to play any material part. Consequently, it is most reasonable to suppose that *the smaller number of high calcium concentrations is due to the fact that these are not cases of affections of the bones*. Just as in the group of active tuberculous processes of bones and joints, the number of high calcium concentrations decreases gradually as confinement to bed goes on — being presumably indicative of a decrease of the activity. The fact that there are no calcium concentrations at all exceeding 330 mg. per litre in the third and fourth half-years is unquestionably a mere accident due to the small number of urines of the 24 hours examined (13 and 12) in these two groups.

On the other hand, the figure 38 *per cent.* of high calcium concentrations in patients with tuberculosis of the soft parts who are out of bed is surprisingly great, though there is no small number of urines of the 24 hours (97). If this figure is more closely analysed, it appears, however, that primarily all the high calcium concentrations were found in only *two* patients — one with periproctie tuberculosis and one with diffuse suppurating cervical glands, both of them with a rather reduced general health and increased sedimentation rate — thus clinically active intoxicating processes. As will be seen, this can explain the figure arrived at — and reduces its universal validity.

Will it be possible now to explain how these deviations from the normal calcium concentration are brought about?

The answer must be in the affirmative.

*Four factors* seem to influence the calcium concentration in the urine:

(1) *The breaking down of osseous tissue.*

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(2) The *intoxication* — through the production of an, at any rate *local*, calcium atrophy of the osseous tissue.

(3) The *confinement to bed* — through the production of a *universal* inactivity atrophy of the osseous tissue.

(4) The *light- and sanatorium-treatment* — through a decrease of the diuresis.

This is confirmed by the figures of the table:

The high figure of *74 per cent.* during the first half year of confinement to bed in cases of active osseous-articular tuberculosis results from a concurrence of all the 4 factors: Breaking down of bone, intoxication, confinement to bed and sanatorium-therapy.

The somewhat lower figure of *55 per cent.* in cases of tuberculosis of the soft parts during the same period of confinement to bed results from the concurrence of only 3 factors: Intoxication, confinement to bed and sanatorium-therapy, whereas the breaking down of bone is not in play.

When only 2 factors — confinement to bed and sanatorium-treatment — concur, as in the cases of inactive tuberculosis of the bones, the figure falls to from *20 to 30 per cent.*

Lastly, the figure falls to *6 per cent.* when only one factor, light- and sanatorium-treatment, is acting as in the cases of inactive osteo-articular tuberculosis who have come out of bed.

So much for the examinations of the *calcium concentration* in the urine.

Examinations with a view to changes of other concentrations in the urine gave the following results:

The *concentration of phosphorus* was quite normal in all groups of patients.

The *concentration of oxalic acid* was slightly increased — not so much, however, that any importance can be ascribed to it in this connection.

The *hydrogen ion concentration* was found to be slightly but distinctly displaced in the alkaline direction in all patients suffering from osteo-articular tuberculosis. This does not influence the solubility of the chief constituent of the calculi, the calcium oxalate, but may be of importance for the admixture of calcium phosphate found in half the number of the calculi.

The results of all these examinations may now be *briefly summarized* as follows:

During the period of the affection of the bone when the symptoms of calculi set on in our patients, we succeeded in demonstrating — in addition to the *favourable possibilities of retention* in the urinary tract — such *pathological changes in the composition of the urine* — in particular an increased calcium concentration — as would favour the precipitation of *just* those substances that were found in the small concentrations discharged. In *other periods of the disease* — and in patients with tuberculosis of the soft parts — such changes were either not found at all or only to a *less degree*, and the possibilities of retention in the urinary tract were, largely considered, *less favourable*. In the few patients in whom *larger calculi* had appeared, the urine and the urinary tract were found to be quite normal.

These results confirm the *hypothesis about the pathogenesis of the calculi in the urinary tract* that had been set up in advance on a more theoretical basis.

According to all that has been ascertained, the so-called primary calculus-formation in the urine can be considered a disease following a course by two stages:

During the *first stage* the possibilities of retention in the urinary tract are so much increased and the composition of the urine is so much changed as to cause precipitation to take place in the urine in the form of small prickly lumps of crystals, or quite small concretions. As long as these changes persist in the urine and the urinary tract, such small concretions are being constantly formed. The majority of these concretions — possibly all — will gradually be discharged in the course of repeated attacks of ureteral colic. After the course of some time the said changes in the urine, and possibly also in the urinary tract, subside and the production of small concretions will cease. If, now, at this time all the small concretions formed have been discharged, then the disease will have come to an end. But if one or several of the small concretions be retained in the urinary tract, the *second stage* of the disease will set on:

The retained small concretions will now continue their growth in spite of quite normal conditions in the urine and the urinary tract. In other words, they act as stone nuclei for the formation of larger calculi. This second stage is thus characterized by the presence of *large calculi in completely normal urine and urinary tract*.

*The first stage* — the one during which the formation of stone

nuclei is going on — may rightly be termed *the actual calculus disease*, as the pathological factors giving rise to the calculus-formation are active only during this stage.

*The second stage* is only a sequela of the actual calculus disease — the pathological calculus-producing factors have now completely disappeared.

In spite of the fact that the first stage must be looked upon as the actual calculus disease, it is far less known than the second stage during which the large concretions are developed. For, quite naturally, it is the large calculi that first and foremost attract the physician's attention.

This view of the pathogenesis of the primary calculus-formation seems to apply at any rate to calculus-formation in patients suffering from osteo-articular tuberculosis. However, it appears to me to be probable that *also other forms* of primary calculus-formation originate from a hitherto unnoticed first stage with constant formation of stone nuclei, caused by transient pathological changes of the concentrations in the urine in connection with favourable possibilities of retention. It should, however, not be overlooked that also other forms of pathogenesis are possible — *e. g.* in conformity with RANDALL's theory.

In conclusion we want to say a few words about the possibility of prophylaxis against these calculi, which constitute so serious a complication in the severe cases of osteo-articular tuberculosis that about 3 per cent. of these patients must submit to operation later in order to have calculi in the urinary tract removed.

At present the possibilities are not great.

Since *the active stage of the osseous affection itself* has so great a share in the calculus-formation, a particularly energetic treatment of the osseous tuberculosis which would soon take the disease into the inactive stage might be justly expected to be the best means of preventing calculus-formation.

Only, it is unfortunate that *the more energetically and consistently* the treatment of the osteo-articular tuberculosis is carried through, *the greater does the risk* of calculus-formation seem to be:

Absolute and strictly maintained rest in the dorsal position and immobilization in patients suffering from spondylitis or coxitis will thus both increase the calcium concentration in the urine and favour the retention of small stone nuclei in the urinary tract. As will appear from our examinations, energetic sanatorium-

treatment and light-baths also seem to favour calculus-formation, probably by influencing the diuresis.

When an intensification of the treatment of the osseous affection increases the possibilities of calculus-formation, it is quite natural that a *slackening of the demands as to treatment will reduce* the risk of calculus-formation. And most of the precautions suggested against calculus-formation in these patients are to the disadvantage of one of the main principles in the treatment of surgical tuberculosis: the immobilization. Changing dorsal, ventral and lateral positions are doubtless excellent prophylactic measures against calculus-formation, but less good for a spondylitis or coxitis present at the same time.

But the fact that the very *treatment of the osteo-articular tuberculosis increases the risk* of calculus-formation involved by the disease in itself *does not apply solely to the methods of treatment hitherto in common use.*

A new line of treatment of tuberculosis has recently been introduced, consisting in treatment with *full doses of vitamin D*. Up to now it has been chiefly employed in the case of lupus, but has also been tried abroad in the treatment of osteo-articular tuberculosis. As far as I know, communications about results have, however, not yet been published.

But one thing is known: A massive vitamin D poisoning — such as is aimed at in this treatment — entails a *considerable increased calcium excretion in the urine*. Considering the results of examinations which we have produced here today, it must be obvious that such a treatment must quite materially increase the risk of calculus-formation in patients suffering from osteo-articular tuberculosis — and this fact should be carefully deliberated by the physician who will attempt a treatment of osteo-articular tuberculosis with vitamin D.

But is it not possible to take precautions against calculus-formation which do not simultaneously reduce the effect of treatment of osteo-articular tuberculosis?

There has been no lack of suggestions there.

Medicinal treatment of varying nature has thus been suggested:

The Swede GRETA HAMMARSTEN<sup>1</sup> suggested the administration of magnesium, and the American SCHORR<sup>2</sup> suggested treatment

<sup>1</sup> Nordisk Medicin 24, 1806, 1944.

<sup>2</sup> The Journal of Urology 53, 507, 1945.

with oestrogenic hormones and with certain aluminium compounds, all aiming at reducing the possibilities of precipitation in the urine. All things considered, it must, however, unfortunately be said that it has not yet been proved that these medicinal treatments exert any effect.

The only prophylactic measure that can be safely recommended at present is actually the modest one to keep the diuresis of these patients at a high level — and this is not even so effective as one might believe, for with increasing diuresis the calcium excretion in the urine increases.

Unfortunately, apart from this easy — but not particularly effective measure, we do not believe that any prophylaxis against calculus-formation in the urinary tracts of these patients is possible at present without slacking the demands that must be made on the treatment of the tuberculous affection of the bones.

But we may hope, of course, that other ways out may appear.

### Summary.

In a total of 748 patients with extrapulmonary tuberculosis treated in the Coastal Hospital at Refsnæs from 1928 to 1939 there were 34 patients with symptoms of urinary calculi in non-infected urine. These 34 patients were all of a group of 176 patients with tuberculosis of bones and joints localized to the vertebral column, the pelvis, the hip- or the knee-joint.

The first symptoms of the urinary calculi — ureteral colic with the passage of small stones — almost always appeared in the course of, or soon after, the active stage of the affection of the bone.

The stones that were passed, or removed, from the urinary tract chiefly consisted of calcium oxalate — in about half the number of cases with an admixture of small proportions of calcium phosphate.

Examinations of the calcium, phosphorus and oxalic acid concentrations in the urine showed that the calcium concentration was considerably increased during the active stage of the affection of the bone — especially so when the patient was being treated at the same time with rest in bed, sanatorium treatment and light-baths. The phosphorus and oxalic acid concentrations were not unquestionably influenced by these factors.

On the basis of the examinations made, the so-called primary calculus-formation in the urinary tract can be looked upon as a disorder manifesting itself by two stages. During the *first stage*, small concretions — stone nuclei — are constantly being formed in the urinary tract as a consequence of *pathologically changed concentrations in the urine*. During the *second stage*, stones or stone nuclei, formed during the first stage but not discharged, increase to form larger concretions *in completely normal urine* and normal urinary tracts.

The first stage must be termed "the actual calculus disease" (and may occur alone). The second stage is just a possible sequela of "the actual calculus disease".

As a rule, however, patients with urinary calculi do not come under treatment in hospital until during the second stage.

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## Un cas de pneumatose kystique intestinale diagnostiqué par la rectoscopie.

Par

KAJ RØJEL.

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La pneumatose kystique (p. k.) est une affection rare. Deux cent cas environ ont été signalés dans la littérature, depuis que BANG (2), en 1876, avait constaté, le premier, cette maladie chez l'homme.

Au point de vue de *l'anatomie pathologique* (1, 8, 12, 13, 17, 22, 25) la p. k. se caractérise par la présence de kystes pleins d'air, localisés, le plus souvent, à l'iléon ou, moins fréquemment, au coecum et au jejunum. Dans de rares cas, les kystes ont été trouvés dans le côlon du côté anal du coecum, dans le duodénum, le mésentère, les ligaments de l'estomac, le péritoine pariétal, et les glandes lymphatiques abdominales. Les modifications peuvent se produire dans toutes les couches intestinales, mais apparaissent le plus souvent dans la séreuse, tandis qu'elles sont moins fréquentes dans la sousmuqueuse et tout à fait exceptionnelles dans la tunique musculaire.

La taille des kystes varie en général entre celle d'un pois et celle d'une cerise, mais on en voit d'infiniment petits et certains de la grosseur d'un oeuf de poule. Ils sont en général uniloculaires, avec une paroi très mince et ne communiquent pas entre eux ni avec la lumière de l'intestin. Ils contiennent de l'air ou — dans de rares cas — un liquide séreux ou du sang. On en voit qui sont pédunculés, mais le plus souvent ils sont sessiles ou intramuraux. Les kystes sont tantôt solitaires, et, dans ce cas plus ou moins arrondis, tantôt, ce qui est le cas le plus fréquent, accumulés en grappe de raisin ou en conglomérats ressemblant à une mousse



Fig. 1.

RØJEL: Un cas de pneumatose kystique intestinale.





de savon, et ils prennent alors une forme polygonale, très irrégulière, anguleuse. De tels conglomerats peuvent devenir très volumineux et engainer la moitié ou d'avantage de l'intestin grêle, de même qu'ils peuvent constituer des masses de la taille d'une tête d'enfant, susceptibles d'être décelés à la palpation.

*Au microscope* (1, 12, 13, 17, 22, 25) la paroi kystique est constituée de minces membranes conjonctives, pauvres en vaisseaux, recouvertes sur la surface interne, par des cellules endothéliales aplaties, plus ou moins cubiques, parmi lesquelles se trouvent souvent de grandes cellules géantes de corps étranger, à noyaux multiples. Le stroma séparant les kystes est souvent le siège d'une infiltration inflammatoire modérée avec des cellules lymphocytaires, des mononucléaires et des éosinophiles.

On admet généralement, paraît-il, que ces kystes proviennent de capillaires lymphatiques par dilatation et étranglement de ceux-ci. (23).

*Apparition:* La p. k. apparaît le plus souvent chez des personnes vers l'âge de 30 à 40 ans et est un peu plus fréquente chez l'homme que chez la femme. On signale dans la littérature quelques rares cas chez des enfants (5, 14).

*Étiologie:* La présence d'une p. k. a presque toujours été découverte accidentellement lors d'une autopsie ou d'une laparotomie faite pour quelque maladie grave. Dans un grand nombre de cas (entre 50 et 75 %), l'affection principale était une sténose pylorique consécutive à un ulcère de l'estomac ou du duodénum (3, 4, 8, 9, 11, 12, 16, 21, 22, 24).

En 1924, NAESLUND (17) a classé les maladies principales des cas publiés jusqu'alors de p. k. de la manière suivante: ulcère vérifié de l'estomac ou du duodénum: 33, signes cliniques d'ulcère, sans que cette maladie ait été constatée avec sûreté: 17, cancer gastrique: 3, appendicite: 3, tuberculose pulmonaire et/ou intestinale: 7, péritonite exsudante: 5, affection cardiaque: 3, anémie pernicieuse: 1, urémie: 1, diphtérie: 1. Dans 13 cas, la p. k. était la seule affection qu'on eût pu constater.

Le nombre élevé d'affections gastriques et intestinales, notamment de sténose pylorique, trouvé parmi les p. k., fait soupçonner l'existence d'un lien causal quelconque entre les deux groupes de maladie; cependant, sur ce point les opinions se heurtent.

Les théories suivantes sur la genèse de la p. k. ont été discutées:

1) La maladie a été considérée comme étant du groupe des tumeurs (2).

2) Des essais sur les animaux ont fait croire qu'il s'agissait d'une avitaminose (7).

3) On a pensé que l'air pouvait être exprimé, d'une manière purement mécanique, de l'intestin et s'infiltrait dans les tissus en traversant une muqueuse ayant déjà subi des modifications pathologiques (3, 11, 15, 19, 22, 23).

4) Enfin, on a considéré la p. k. comme une maladie infectieuse (17, 20).

Actuellement, la théorie selon laquelle la p. k. serait une maladie d'origine infectieuse, semble rallier le plus grand nombre de suffrages, bien qu'il faille admettre que la question de l'étiologie de la maladie reste encore à résoudre de manière définitive.

*L'aspect clinique:* Comme nous l'avons déjà dit plus haut, la p. k. a le plus souvent été constatée simultanément avec une affection gastrique ou intestinale grave et n'a pas donné de symptômes subjectifs propres. Dans de rares cas, chez des malades accusant de vagues troubles dyspeptiques chroniques, on n'a rien pu déceler d'anormal que la présence d'une p. k., ce qui a fait attribuer à cette affection les symptômes dyspeptiques. Dans d'autres cas, également rares, il existait un iléus causé par des brides ou des coudes intestinaux qu'on a pensé attribuer à la p. k. décelée à l'opération ou sur la table d'autopsie. Un cas isolé de p. k. a été rapporté, où des grands kystes sousmuqueux ont provoqué un iléus d'occlusion.

Tout compte fait, il faut dire que l'affection ne présente point de symptômes, ou que les signes subjectifs qui l'accompagnent sont si vagues, qu'à eux seuls ils ne font guère penser à cette maladie. La description des signes objectifs sera remise à l'exposé du diagnostic.

*La prognose* est bonne. Lors de relaparotomies, on a pu constater, dans plusieurs cas, la disparition complète en quelques mois des kystes pleins d'air trouvés au cours d'une opération antérieure; les seules traces qui en restaient, étaient de petits épaissements et des cicatrices blanchâtres sur la séreuse (4, 10, 11, 12, 16, 23). Bien qu'il soit probable que l'air, à la rupture des kystes, puisse pénétrer dans le péritoine, il est exceptionnel de voir des ruptures intestinales et des péritonites par suite d'une p. k. (13).

*Traitement:* Les cas simples de p. k. ne demandent pas de traitement, et il est même contreindiqué de tenter l'ablation des kystes par une résection ou de semblables interventions risquées, si on venait à la diagnostiquer lors d'une laparotomie. Si la p. k. donne

lieu à un iléus, il faut circonvenir l'occlusion par une anastomose.

*Diagnostic:* Nous avons déjà dit que l'anamnétique de la p. k. est peu caractéristique et permet difficilement d'établir un diagnostic précis. L'examen clinique ne suffit pas non plus. Citons toutefois, à titre de curiosité, qu'on a pu, dans un cas, déceler une intumescence molle, crépitante, qui s'est révélée à l'opération être un grand conglomérat, constitué de kystes pleins d'air (16).

Or, ces dernières années, on a pris connaissance de certaines modifications radiographiques caractéristiques, qui permettent de poser le diagnostic par un examen aux rayons X.

Dans certains cas (4, 6, 8, 9, 21, 24), on a pu voir directement sur la radiographie de l'abdomen les kystes pleins d'air comme de faibles éclaircissements arrondis ou anguleux, limités et séparés entre eux par des lignes très fines formant comme un réseau. Habituellement, les éclaircissements sont de la taille d'un pois ou d'une cerise, ils sont serrés et superposés et donnent l'impression d'une structure mousseuse. Dans d'autres cas, les éclaircissements sont en général plus grands, plus espacés et moins nombreux et sont alors susceptibles d'être pris pour des éclaircissements dus à une accumulation d'air intrainestinal. Le manque des valvules conniventes de Kerckring et des boursouflures intestinales dans les éclaircissements causés par une p. k., permettra dans les cas douteux d'établir un diagnostic précis. Tantôt les modifications sont très limitées, tantôt elles occupent une grande partie de l'abdomen.

Bien que cette affection ne trouve pas dans l'abdomen un lieu de prédilection précis, il est remarquable que les anses intestinales atteintes de p. k. sont sujettes à monter et à s'interposer entre le foie et le diaphragme (6, 8, 21, 22, 24). Cette interposition est généralement réversible. Quelquefois, on ne voit que l'anse intestinale interposée, sans qu'il soit possible d'observer les éclaircissements spécifiques. Or, même cette image doit éveiller les soupçons.

La plupart du temps les cas assez prononcés pour que les modifications dues à la p. k. puissent être observées directement sur la radiographie, présentent un pneumopéritoine avec toutes les caractéristiques radiologiques bien connues (6, 8, 21, 22).

En parcourant la littérature, je n'ai réussi à trouver que deux observations de kystes pleins d'air, où les auteurs décrivent des altérations radiologiques. Dans l'un des cas (3), il existait dans

l'estomac et dans le duodénum une pneumatose sousmuqueuse prononcée, ressemblant, après ingestion opaque à une «éponge imbibée de baryte». Dans l'autre cas (25), on put déceler, après lavement opaque, une p. k. dans le colon descendant et transverse sous forme de déféctuosités arrondies ou plus irrégulières, de la taille d'un pois, séparées les unes des autres par des prolongements dentiformes de l'ombre du contraste.

Ce n'est que dans de rares cas (3, 6) qu'on a pris en considération, lors de l'examen radiographique, l'image caractéristique que nous venons de décrire. Dans les autres cas, le diagnostic a été établi à l'opération ou bien lors de l'autopsie et après cela seulement une révision des radiographies a permis de reconnaître les altérations typiques.

La p. k. ne nécessitant pas une intervention chirurgicale, le radiodiagnostic sera dans la plupart des cas inutile à une exception près. S'il existe un pneumopéritoine chez un malade atteint d'ulcère stomacal, on risquerait — comme il est arrivé quelquefois — d'établir un faux diagnostic: perforation de l'estomac, et de soumettre inutilement un malade peut-être faible et déshydraté, à une laparotomie aiguë. Si on envisage un tel cas de pneumopéritoine sans signes cliniques de perforation, on fait bien d'étudier de très près les radiographies, ce qui permettra peut-être de trouver les éclaircissements arrondis, qui sont la caractéristique indubitable de la p. k. et avec cela l'origine de l'air libre dans le péritoine.

La p. k. ne semble jamais avoir été diagnostiquée par une rectoscopie, et je crois donc que l'observation qui va suivre pourra comporter quelque intérêt.

Il s'agit d'une femme âgée de 39 ans lors de son entrée à l'hôpital départemental et municipal d'Odense en mai 1944. Pas d'antécédents pathologiques. Seize mois avant son admission au service, des symptômes intestinaux s'étaient produits sous forme de constipation et de diarrhée alternées. Une fois les selles contenaient du sang frais. Elle eut ensuite pendant une période de 4 à 5 mois des diarrhées violentes accompagnées de fatigue et de perte de poids mais sans présence de mucus ni de sang dans les selles. Puis les troubles cessèrent spontanément, et la malade se portait bien jusqu'à un mois avant son hospitalisation, où la constipation et la diarrhée alternées recommencèrent. De même elle remarquait de temps en temps du sang ou du mucus dans les selles.

Parmi les examens faits au service, je me bornerai à parler de la

rectoscopie et de l'examen aux rayons X du côlon, les autres ne présentant rien d'intéressant.

«A la *rectoscopie*, la muqueuse est à peu près normale jusqu'à une hauteur de 15 cm. A partir de cet endroit commence une affection consistant en des nodules couvrant toute la circonférence intérieure de l'intestin. Les nodules peuvent atteindre la taille d'un pois et même peut-être d'avantage. Ils ressemblent à des kystes et sont minces comme du papier au sommet. La formation noueuse s'étend jusqu'à une hauteur de 25 cm, mais au-delà l'examen est impossible. D'après l'apparence des nodules, il pourrait s'agir de kystes muqueux, mais quand on en perce deux au sommet, ils se dégonflent sans qu'on voit de mucus. Ils doivent donc être remplis d'air.»

A l'*examen radiographique subséquent du côlon*, la radiographie d'ensemble a montré, localisées au petit bassin, de nombreuses bulles d'air presque circulaires, dont la taille varie entre une pièce de 1-ore et une de 2-ore. Elles se différencient de l'air intestinal par une grande homogénéité et une délimitation nette, chaque bulle étant entourée et séparée des autres par un «septum» distinct. Un examen après lavement opaque (fig. 1) ne décèle aucune abnormité au rectum.

Les contours sigmoïdes présentaient une image curieuse avec de nombreuses impressions rapprochées, hémisphériques, en partie confluentes. Celles-ci qui répondaient exactement en taille et en forme aux bulles d'air de la radiographie d'ensemble, pouvaient être observées telles quelles sur toute les photographies. Les altérations étaient localisées au sigmoïde et n'atteignaient pas le côlon descendant. Les autres parties du côlon étaient normales.

Lors d'un *examen supplémentaire* en septembre 1947, la malade nous dit avoir remarqué à des intervalles très espacés, un peu de sang frais dans les selles. A cela près, les selles étaient parfaitement normales, journalières, spontanées, sans aucune gêne, et la malade était en très bon état de santé.

A la rectoscopie, l'aspect était nettement identique à celui trouvé en 1944.

L'évolution de l'affection pendant les trois années et demie postérieures à 1944, de même que l'image rectoscopique restée identique, témoignent de ce que la pneumatose à elle seule n'a donné d'autres symptômes que la présence rare et peu abondante de sang dans les selles.

L'hospitalisation en 1944 a probablement été précédée par une colite. Il reste à savoir si la colite a été causé par la pneumatose, ou si la pneumatose kystique a simplement été primaire et la colite secondaire.

### Summary.

Cystic pneumatosis is a rare disease, which is characterized by the formation of gas-filled cysts in the intestinal wall in size varying from that of a pea to that of an egg.

The author reports a case of cystic pneumatosis, the diagnosis of which was made through proctoscopic examination, which revealed thin-walled gas-filled cysts, about the size of a pea and localized in the mucous membrane of the rectum, the lesion beginning 15 centimetres above the anus.

In roentgenograms of the abdomen, taken without the administration of contrastsubstances, numerous round superimposed gasbubbles were observed in the pelvis. Roentgenograms following barium enemas showed round defects in the shadow of the sigmoid colon, corresponding to the above mentioned gasbubbles (fig. 1).

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## Barge-Bourgain's Reaction in Genito-urinary Tuberculosis.

By

O. SIEVERS and TH. BERGLIN.

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### I.

#### Experimental Studies.

By

O. SIEVERS.

*Introduction and Technic.* In 1946 PIROT, BARGE and BOURGAIN reported on the results of a reaction previously found by BARGE and BOURGAIN with sera from patients suffering from tuberculosis. The reaction, termed BBR in this paper, is produced in the following manner:

Fresh active patient serum is injected around the lymphatic glands of guinea pigs infected with tuberculosis. The animals are injected with tuberculous material preferably 10 days—several months prior to the injection of serum so that the inguinal lymphatic glands may have time to swell. In order to render possible reactions more conspicuous, animals with light-coloured coats should be chosen, and before the experiment is performed the hair around the inguinal lymph nodes is shaven off. With the aid of a hyperdermic needle inserted subcutaneously in an area of the abdomen which is free from glands the patient's serum, 3—6 ml. according to the size of the animal, is injected in very small portions around the tubercular lymph nodes. Healthy guinea pigs with light coloured coats and of roughly uniform size are given equal injections of serum into correspondingly similar areas. During the first 10—15 minutes an animal thus injected is extremely unquiet and the shaven area around the nodes will often show a rash. BARGE and BOURGAIN consider such a reaction in the lymphatic region 8—12 hours after injection to be a sign of positivity, provided, of course, that the control animal does not concomitantly display corresponding

changes. The intensity of the reaction is indicated by the above mentioned workers in the following manner:

1) a weak reaction (+) is characterized by a slight reddening of the glandular region and is only recognizable when compared with the negative control animal,

2) a positive reaction (++) shows a distinct reddening and swelling of the lymphatic region, and is readily manifest without such comparison,

3) a strong reaction (+++) is indicated by an extensive and intensive reddening with edema, and the glands are substantially swollen, whilst finally

4) a very strong reaction (++++) reveals a hemorrhagic reaction spread over the whole of the swollen lymphatic area and, as a rule, the animal dies within a day or so. In cases in which the reaction is weaker than (+) or in which also the control animal displays a similar reddening, a new test should be performed.

PIROT, BARGE and BOURGAIN, and later also DA SILVA, contend that the reaction is positive in patients suffering from tuberculous peritonitis, pelveoperitonitis and pleurisy, and that sera from patients with pulmonary tuberculosis likewise may react positively. They also believe the reaction to be of direct diagnostic significance in tuberculous epididymitis, adenitis, and abscesses.

As an explanation of this reaction BARGE and BOURGAIN assume the escape of various products or toxins from the tuberculous process into the blood stream. They assert that the reaction these products are capable of bringing about in guinea-pigs is not identical with the tuberculin reaction, and point out that the latter test will give a positive reaction even a few days after the actual injection, whilst a positive BBR reaction will generally change to negativity within 24 hours. They also point out that in human beings sensitivity to tuberculin will persist throughout the whole of life, whereas BBR may sometimes be positive and sometimes negative in one and the same patient, dependent upon the stage of the tuberculous process. On the occasion of a test, the tuberculous process must be in the healing stage, or so encapsulated as to inhibit the escape of such products into the blood stream, or the tuberculous nest must be giving off the products in question, which are then liable to enter the circulatory system. If the latter be the case, the above mentioned authors consider the disease to be in a labile stage, from which they infer that a tuberculous patient ought not to be operated on as long as the BBR is ++ or stronger. When drawing this conclusion BARGE and BOURGAIN have in mind above all urogenital tuberculosis,

in which disease they consider the reaction to be of great clinical significance. In confirmation of the view upheld by BARGE and BOURGAIN, DA SILVA reported from Dos Santos Clinic, Lisbon, two cases of tuberculosis of the urogenital system in which the patients post-operatively developed general tuberculosis. Both cases underwent operation at a time when the BBR was strongly positive, whilst all the patients operated for a similar disease with a neg. BBR on the occasion of the operation survived without complications. According to BARGE and BOURGAIN, a neg. reaction does of course not exclude a tuberculous affection but only constitutes a sign that the products in question are not passing from possible tuberculous nests into the blood stream, or if so, in quantities too small to be demonstrated in guinea-pigs.

In the experiments the author performed with this reaction the same technic was applied as that used by earlier workers. Some of the guinea-pigs were infected with a pure strain of *tb. bacillus of the human type* 14 days before the serum injection, whilst others were infected about six weeks prior to the BBR test with sputum or gastric washings containing *tb. bacteria*. The animals were equally suitable in both cases, although the positive reaction in the guinea-pigs infected a fortnight prior to the test with a pure strain were inclined to be stronger, which was to be expected. Furthermore, the use of guinea-pigs injected only 14 days before testing eliminates the necessity of having to read the reaction repeatedly. As a rule, the serum was injected in the evening and the reaction read early the following morning. For some unaccountable reasons a number of the animals died over night. It was without exception always the *tb. infected animals* that died, and their deaths were probably due to the fact that the injection was too great a strain for them, or the insertion of the needle had caused such lesions as were too great for the animals to survive. But in such cases and in those which the control animal shows local changes in the injected region the test should be repeated with new specimens of serum. It should also be observed that too large an injection of serum in a single region is liable to lead to subcutaneous hematoma and thus render the reading of the reaction difficult or even impossible.

*Examinations with clinical material.* According to reports of earlier investigations sera from patients with pulmonary tuberculosis will react positively. With a view to gaining personal experience with BBR, sera was examined from 19 different patients

with pulmonary tuberculosis, all of which had been hospitalized on the preceding day on account of a deterioration in their tuberculous condition. Clinically, they were all in the active stage of the disease. Sera from 9 of these patients gave BBR +++, 4 gave BBR+, 3 were negative, and in three cases the control animal exhibited a local reddening, for which reason the reaction could not be evaluated. All three of the BBR negative tests were of patients with recently diagnosed pulmonary tuberculosis with short histories. In two cases recently diagnosed patients reacted BBR+++ and +, respectively. The remaining cases consisted of patients whose tuberculosis had been diagnosed much earlier and who had been re-admitted on account of a deterioration of their illness. The sera of those patients who reacted positively were re-examined every 10—14 days until they reacted negatively. It was observed that the change from positive to negative was relatively slow, many of the strongly positive cases not becoming negative until after an elapse of about six weeks, whilst those reacting weakly were neg. after approximately four weeks.

*Experimental examinations.* It is not my intention to discuss to what extent a positive reaction supported by the accumulated experience gained on the whole of our material warrants diagnostic significance, or whether the result of a BBR should influence the decision of the therapy to be adopted, but would in this respect and in clinical questions refer to the clinical material published by BERGLIN in the same copy of this journal. In an attempt to provide an experimental basis for the discussion of the possibly specific type of the reaction, the author will instead describe some experiments performed on guinea-pigs with tubercular bacterial cultures.

PIROT, BARGE and BOURGAIN contend that a guinea-pig will not react positively if injected around the glands with 1) a pounded tuberculous gland, 2) urine containing pus and tubercular bacteria and excreted from a patient with a tuberculous affection of the kidneys despite the fact that serum from the same patient may possibly react BBR positively, and 3) 1 mg. and 1 cg. respectively, of tuberculin. Even if the above mentioned type of material does not react BBR positively, one might nevertheless imagine that various types of tb. cultures might do so. But this would not constitute evidence that products appearing in the patient's blood originated from the actual bacteria and not from the tissues of the host, but we might possibly learn that reactions similar to BBR may be obtained by products which most certainly

do come from the bacteria. With this in mind, the first thing the author did was to inject Besredka, Sauton and Dubos substrates into guinea-pigs with tubercular glands. Sterile substrates of this nature produced no reaction, whilst those substrates on which tb. had been allowed to grow reacted in different manners. In these experiments the cultures were always first centrifugated at about 3,000 r. p. m. for half an hour after which the clear centrifugate was injected in undiluted condition into the animal in the usual manner. As is known, the bacteria grow very rapidly on Dubos substrate. An injection of a centrifugated, two week-old substrate did not produce any reaction. Only once was the author able to show a weak reaction (+) with a substrate after the growth of a pathogenic strain of the human type. The centrifugates of two week-old Sauton cultures of both a pathogenic human strain and a B. C. G. culture produced a similar, slight reaction, whereas the centrifugate of one month old Besredka-cultures showed strong positive reactions (+++ and ++) respectively. The control animals were altogether unaffected. An injection of the centrifugate of these substrates on which coli- and staphylococcal cultures had grown always produced a more or less similar reaction both in the tuberculous and in the healthy control animals. In the injected substrates on which tb. cultures have been grown there must exist products that arise in association with the growth of the bacteria. The longer the bacteria had been allowed to grow in the substrate, the stronger was the reaction. In this conjunction the author would also mention that the pH of the substrate was always determined and the small deviations recorded cannot be held responsible for the reaction. If the pH value had played any substantial rôle, also the control animals would have reacted. In the experiments different strains were used, both of human and bovine types.

In a further attempt to elucidate the causal factors of these BBR-like reactions obtainable with different substrates, the author performed the following experiments: A three week-old Sauton culture of a pathogenic tb. bacillus strain of human type was centrifugated and the centrifugate stocked. Some of the 'dry' bacteria in the sediment were suspended in saline, whilst others were carefully pounded with fine sand in a mortar and after the admixture of a suitable quantity of saline, centrifugated. The various centrifugates or bacterial suspensions were then inoculated in the usual manner in the glandular regions. Three (3)

ml. bacterial suspensions (approx. 100 milliard/ml.) gave no reaction in BARGES and BOURGAIN's conception of the word. 3.0, 1.0 and 0.5 ml., respectively, of the centrifugate killed the tuberculous guinea-pigs within 4—24 hours, without any precursory reddening being observable around the glands. The healthy control guinea-pigs did not react at all. 0.15 ml. of the centrifugate gave on the other hand a fairly typical BBR with reddening and swelling of the lymphatic region. Also in this case were the control animals negative. The heavy doses of the centrifugate were too toxic and this might possibly explain why some of the animals, as pointed out above, died within a few hours after being injected with the patient's serum. It is possible that the serum in these cases contained too much of the products in question and that the animals therefore died from overdosing.

For comparative purposes, a number of guinea-pigs were injected with tuberculin (a mixture of human and bovine) 1.0 ml. undiluted tuberculin produced a positive reaction (++) in the tuberculous and in the healthy guinea-pig. Two days later the healthy animal reacted negative whilst the tuberculous animal reacted positive still after three days. Half the amount of tuberculin, *i. e.*, 0.5 ml. undiluted tuberculin, gave a weak reaction (+). In this case the control animal was negative. Still smaller doses of tuberculin produced no reaction in the animals. The results obtained seem to confirm BARGE and BOURGAIN's assertion that BBR and the tuberculin reaction are not identical. The products responsible for the BBR may contain tuberculin, but so far they cannot be considered as consisting of tuberculin only. In all probability there must exist here not only a quantitative but also a qualitative difference. In this respect it should be borne in mind that the animals used for the BBR tests had been infected with tb. only 10—14 days before the injection of serum. At the time of the experiment the animals were Mantoux neg. For this reason the animals cannot be expected to react so strongly as in the usual standardized tests with tuberculin.

Finally it might be observed that despite repeated tests serum, 3 ml., from guinea-pigs infected with tuberculosis produced no positive BBR reaction when injected into other tuberculous guinea-pigs. The serum used for these experiments had been taken from guinea-pigs with small, insignificant inguinal glands, as well as from guinea-pigs with large necrotic patches at the site of formerly visible tuberculous glands.

*Summary.* The present examinations show that it is possible with the use of material containing the decomposed substances of tb. bacteria, to obtain a reaction similar to that shown by BARGE and BOURGAIN in guinea-pigs infected with tuberculosis and injected with serum from tuberculous patients. In these experiments substrates were used on which tb. cultures had been grown, and tb. cultures that had been carefully pounded. Living tb. suspended in a physiological salt solution will not produce such a reaction in the animal. No evidence was produced to show that it was the same substances as appear in the serum of some patients, when the guinea-pig tests are pos. in BARGE and BOURGAIN's conception of the term. It can only be stated that the reactions in both cases exhibit similar pictures and that it is not incredible that the two substances are identical. If this is the case, this might be accepted as a sign that BARGE and BOURGAIN's reaction really is a specific reaction. Tuberculin can give a similar reaction, but only on condition that the animal be given a minimum quantity of 0.5 ml. undiluted tuberculin.

The difference between BARGE and BOURGAIN's reaction and the tuberculin reaction is not only quantitative but in all probability also qualitative. It should also be observed that it is not yet known whether similar products might possibly be manifestable in cultures of other bacteria besides the examined coli and staphylococcal cultures, which have not such substances.

## II.

### Clinical Experience with Barge-Bourgain's Reaction.

By

THORWALD BERGLIN.

In urogenital tuberculosis, as also in other forms of tuberculosis, operations should preferably be performed at a time in which the tuberculous infection is in a quiescent phase in order to diminish the risk of such an operation causing a direct spreading of the disease. Experience has shown, however, that it is often extremely difficult to choose the suitable moment. By recording the course of the disease, existing symptoms, E. S. R., temperature, possible changes in the blood, etc., certain information of the condition of the patient at a given moment is available. The information



thus obtainable is however often inadequate and sometimes even misleading. New examination methods are therefore sorely needed, methods giving reliable and more detailed information on the state and nature of the tuberculous process. It was therefore with great interest that we learned of the results of BARGE-BOURGAÏN's, as well as DA SILVA's investigations, which seem to argue for the reaction described by them being a valuable addition to our clinical arsenal for the evaluation of a possible activity of the tuberculous process. In order to gain experience with and to judge the practicability of this reaction the author tried it clinically and endeavoured to find out if it is specific for tuberculosis and also discussed its value from the diagnostic point of view and secondly sought to form an opinion as to its value in judging a possibly existent activity of a tuberculous affection, and thereby also evaluate its possible usefulness as a tool for determining the most suitable moment for a possible operation. The whole material consisted of 111 cases, and has been divided into three groups apparent from the following table. The control material consisted of non-tuberculous diseases in the urogenital system and other non-tuberculous diseases.

Table 1.

*The Whole Material Divided into Groups According to Diagnosis and Strength of BBR, Respectively.*

	Nr. of cases.	BBR +++	BBR ++	BBR +	BBR —	Unclear reaction
A. Tuberculosis:						
Clinically clear urogenital tuberculosis (except epididymitis) .....	22	2	6	5	9	—
Tuberculous epididymitis .....	9	—	3	3	3	—
Pulmonary tuberculosis	19	9	—	4	3	3 <sup>1</sup>
Tuberculosis of other organs .....	10	—	1	1	8	—
Clin. suspected urogenital tuberculosis (except epididymitis) ..	1	—	—	—	1	—
Clin. suspected epididymitis .....	7	1	2	3	1	—
Doubtful cases .....	1	—	—	1	—	—
B. Non-tuberculous diseases in the urogenital system	17	—	—	—	17	—
C. Other non-tuberculous diseases .....	25	—	—	—	23	2 <sup>1</sup>
	111	12	12	17	65	5 <sup>1</sup>

<sup>1</sup> Control animal showed a rash, for which reason the reaction could not be judged.

Is BARGE-BOURGAIN'S reaction specific for tuberculosis and can it as such warrant diagnostic significance? This is the question to be answered first. As will be apparent from the above table the reaction is not always positive from a specific-diagnostic point of view. In 60 patients with clearly diagnosed tuberculous affections the reaction was primarily negative in 23 cases (= 38 per cent.). This agrees well with BARGE-BOURGAIN'S result and can be explained by the natural variation in the activity of the tuberculous process, if we assume the nature of the reaction to be that advocated by the above mentioned authors and confirmed by our own experimental examinations. Of the 41 patients that primarily reacted positively, 34 were from the beginning clearly tuberculous or were later found to be so. Six cases, 5 of which were epididymitis and 1 aseptic pyuria, had been strongly suspected of tuberculosis clinically, and a positive Mantoux test showed that the patients were infected with tuberculosis. In the remaining case — an epididymitis — recorded in the table as doubtful no direct support for the specificity could be produced, the course of the disease, however, did not argue against tuberculosis. A repeated Mantoux test in this case was unclear (1 mg. reaction  $6 \times 8$  mm.)

The last seven cases must be discussed more at length from a specific-diagnostic point of view. Other clinical methods have hitherto not been able to produce conclusive evidence for the diagnosis 'tuberculosis' in any of these cases. So far, only one case of epididymitis has been operated on, and microscopy did not reveal any signs in favour of tuberculosis, which does not however exclude this diagnosis. The chronic course of the cases does admittedly not give any definite indication of the nature of the disease but on the other hand it does not argue against the assumption of a tuberculous affection. The fact that the epididymitis had in some cases disappeared completely at re-examination may seem to argue against tuberculosis, but such regression is sometimes met with in tuberculosis. The histories of the seven cases will be given in brief in the following.

In one case a strongly positive reaction was recorded (+++):

*Case 1. Male, 21 yrs.* For a year or so periodical precipitant urination. 5 days pains and tenderness of right epididymis. Admitted 25. 1. 47 on account of slight rise in temp. during last 24 hours. Local status: Right epididymis hard, enlarged, somewhat tender, vas deferens swollen, tender. E. S. R. 4/13. Urine: 0 tbb., sed: 0. Gc. cultivation:

neg. Urography: neg. Pulm.: 0. Guinea-pig test: neg. Mantoux: pos. BBR 28. 1. 47 + + +, 28. 2. 47 hardening of cauda epididymidis still persistent. Epididymectomy: histological diagnosis: no evidence of tuberculosis. Three weeks after op. a large, very nodose, and not tender resistance was found at the site of the earlier epididymis. Two months later the swelling had become smaller. At re-examination 9. 12. 47 hematuria was established and X-ray examination showed suspected tuberculous changes in the middle calyx of the left kidney.

In two cases the BBR was positive (+ +):

*Case 2. Male, 18 yrs.* BCG-vacc. 4. 11. 46. Mantoux Jan. 47 pos. 1 mg. 10 × 12 mm. Admitted 13. 3. 47 with fever and tender epididymis. Local status: Right epididymis hard, swollen, not tender. E. S. R. 20/41. Urine 0 tbb. Sed: 0. Guinea-pig test: 0. Gc. cultivation: neg. BBR + +. 2. 4 slight persistent swelling of cauda epididymidis dx. At re-examination of patient on 3. 12. 47 there was locally hardly any of the earlier infiltrate left, possibly an increased hardness as compared with the other side. Urography: neg. Mantoux 1 mg. now produced a very strong reaction with a pronouncedly edematous reddened zone covering almost the whole of the lower arm.

*Case 3. Male, 26 yrs.* Sister and brother tb. pulm. For some time precipitant urination, and was therefore admitted to hospital on 15. 3. 47. Local status: Right cauda epididymidis walnut-sized, hard, nodose, not tender. E. S. R. 8/18. Urine: 0 tbb. Sed: 0. Guinea-pig test: neg. Gc. cultivation: neg. Urography: neg. BBR 21. 3 + +. Mantoux pos. At re-examination 5. 12. 47 cauda epididymidis was still hard and nodose. Pulm: 0. Urography: neg.

In four cases the BBR was weakly positive (+):

*Case 4. Male, 44 yrs.* Jan. 47 a few days slight pains in the back. Applied for health certificate on 5. 2. 47 when Alb. +, admitted 13. 2. 47. Urine: 0 tbb. Sed.: aseptic pyuria. E. S. R. 2/6. Mantoux pos. BBR +. Urography: very strongly suspected cavernous changes in the cranial group of calyces in the left kidney. Guinea-pig test: neg. 9. 4. 47 aseptic pyuria still existent. Since then patient has been at sea and could not be re-examined.

*Case 5. Male, 43 yrs.* Nephew died of tuberculosis. Jan. 47 epididymitis. Hospitalized 12. 3. 47 on account of three weeks' precipitant urination, and tenderness of right epididymis. Local status: two pea-sized tender nodes in the cauda epididymidis dx. Prostate: locally hard, not tender. Sed: 0. Urine: 0 tbb. E. S. R. 3/8. Mantoux pos. BBR +. Urography: neg. Re-examination 30. 9: still hardness of prostate. 5. 12 Hematuria, epididymis still exhibits swelling. Urography: neg. Pulm. X-ray: neg.

*Case 6. Male, 19 yrs.* For 6 days pains in left epididymis. Admitted 10. 5. 47 Temp: 0. Local status: Moderately tender left epididymis, the size of a hen's egg. E. S. R. 22/52. Mantoux pos. Urography: neg. Urine: 0 tbb. Sed: 0. Guinea-pig test: neg. BBR +. 3½ weeks later only very slight regression. Re-examination 10. 12. 47

revealed local, very pronounced testicular atrophy; the only rest of the epidymis and testis was a bean-sized node.

*Case 7. Male, 22 yrs.* Two weeks swelling, pains and tenderness of left epididymis. No secretion from urethra. No urinary tract trouble. Admitted 17. 3. 47 for his epididymitis. Local status: left epididymis nodose, hard, not tender. The caput almost the size of a walnut. Vesicula seminalis sin. was felt like a hard cord, somewhat nodose. Sed.: moderate amount of white blood cells. 0 tbb. Gc. cultivation neg. E. S. R. 5/18. Guinea-pig test: neg. Urography: neg. BBR +. 3. 4: Palpation finding in vesicula seminalis disappeared. 15. 5 epididymitis regressing but some infiltrate still left in cauda epididymidis. Mantoux 1 mg. repeated doubtful  $6 \times 8$  mm.

Although the first case was clinically strongly suspected, we decided not to include it in the clearly tuberculous group because no bacteriological diagnosis has yet been obtained.

Case 2 was placed in the suspected group because it reacted strongly to Mantoux test. It seems to us to be quite inexplicable how a B. C. G. vaccination one year previous should be capable of producing so strong Mantoux reaction. In all probability a tuberculous infection must have supervened in the meantime. Very careful examinations of the patient have however not been able to show any pathologic changes at all except the epididymitis in question.

Case 3 should be considered a case of suspected tuberculosis not only on account of the very strong tuberculous predisposition but also on account of the persistent hard infiltrate in the epididymis in the absence of urethritis in the history or on admittance besides which the Gc. cultivation was negative. The patient has not yet been operated on.

Case 4 showed X-ray changes in one of the kidneys, but as the bacteriological diagnosis has not yet been established and as a later re-examination could not be performed, also this case must for the time being be classed among the clinically suspected ones.

Case 5. Hereditary predisposition and a prolonged chronic course with persistent infiltrates inter alia in the prostate in this case point towards tuberculosis (LJUNGGREN, JÄRVINEN) and do not argue against BBR.

In case 6 a slow regression is suggestive of tuberculosis, at any rate it does not contradict BBR.

As to the last case, recorded in the table as doubtful, it was possible to exclude Neisser with great probability. The vesiculae seminales were involved but the infiltrate regressed

relatively quickly. No clear evidence for tuberculosis could be produced.

In none of these seven cases, however, did the short observation time permit us to assert that the BBR was misdirecting, and as long as we are unable clearly to explain the etiology of the individual cases, such misdirection cannot be proved. The suspicion of tuberculosis must stand. *Of all of the 41 cases with pos. BBR reactions there was only one in which tuberculosis was really doubtful.*

This case, however, was one of the very first cases and recorded as weakly positive and so it is possible, that the reaction may not have been positive but only registered as such on account of lack of experience with the method. The fact is that by a very slight reddening even in guinea-pigs with light-coloured coats it may be difficult to judge, if weakly positive or negative. Experience therefore is necessary.

As will be apparent from the table, the *BBR in all of the 17 controls consisting of non-tuberculous cases of the urinary tract was negative.*

Likewise, *all of the 23 judgeable controls consisting of non-uro-genital cases were clearly negative.* These cases included inter alia, infectious diseases, cancer, ulcer ventriculi, thrombosis, Grave's disease, and purpura thrombocytopenia. As our examination showed that a pre-operative BBR neg. may change post-operatively to positivity in tuberculous patients the BBR was tested on 13 non-tuberculous controls after rather large operations such as nephrectomy, resection of the stomach, splenectomy, cholecystectomy, prostatectomy, explorative laparotomy, and thyroid resection, but *all with negative results.*

On the basis of the above facts the author considers that the *examinations argue for Barge-Bourgain's contention that the BBR is specific from a diagnostic point of view.*

As to the diagnostic value of the reaction, BARGE and BOURGAIN assert without however discussing or describing the course of the reaction, that it is in several tuberculous conditions positive and of direct diagnostic significance. As the time and the course of the reaction will be discussed further down, I will not dwell on them here, although it should already now be pointed out that, as will be apparent from the above, *only a positive reaction is of diagnostic value.* In virtue of its specificity the reaction seems to be of significant value, especially in those cases in which bacteriological or

histological evidence of tuberculosis is wanting, as is often the case in epididymitis and hematuria.

It is also apparently invaluable in the establishment of an *early diagnosis* in obscure cases of the urinary tract. In a number of cases of renal tuberculosis in this material the BBR was *immediately* suggestive of a specific diagnosis which could not be confirmed by the bacteriological examination until *much later*. It is also of certain interest to note that in some cases, later renal changes were detected only at re-examinations indicated solely by the BBR reaction, a fact which also shows how desirable it is to follow up a patient with a positive reaction over a sufficient span of time and until the causal factors of the reaction have been accounted for.

It is however above all in the determination of the developmental phase and possible activity of a tuberculous infection that the BBR is expected to be invaluable. In certain cases blood from patients with tuberculous infections gave a negative BBR reaction. Is this always a sign that the tuberculous process is in an inactive phase? Probably not, it being quite conceivable that even in the active phase there may be cases in which the registrable products escaping from the tuberculous processes are wanting in the blood on the occasion of the examination either on account of a possible "critical limit", under which they cannot be recorded — and thus a limit under which we cannot register the activity — or on account of the excretion from the process being only periodic. A perusal of the material will show that in 8 of 16 primarily BBR-neg. cases certain signs of activity existed, but three of these cases were hard to judge on account of another infection in tuberculous fistulas.

On the other hand, 14 of 15<sup>1</sup> primary BBR-pos. urogenital cases showed signs of activity, or revealed activity in the later course of the disease. The 13 BBR-pos. cases of pulmonary tuberculosis were *all* in a clinically active stage. The 2 BBR-pos. cases located elsewhere were *both* in an active stage. *Of 30 primarily BBR-pos. cases there was thus but one case that did not show any signs of activity.* This warrants the following conclusion:

*If the BBR is pos. it argues strongly for a tuberculosis in the active stage.*

The value of the reaction as an indicator of the activity of a

<sup>1</sup> Remaining 4 cases were sec. BBR-pos.

tuberculous infection was very conspicuous in those cases in which a pos. BBR was not accompanied by clinical signs of activity, but in which the later course of the disease revealed a distinct activity of the process.

As pointed out further up, a negative BBR does not exclude the existence of an active tuberculous process. *If the BBR is negative, tuberculosis in the active stage can be present.* This will be apparent also from the fact that BBR rapidly changes to negativity by rest, to which the author shall revert further down. The material includes in the group "Tuberculosis located elsewhere": lymphoma colli, ileitis, gonitis and spondylitis tuberculos. In this group we have — in spite of clinically demonstrable activity in the majority of cases — the greatest number of negative BBR, and our material does not correspond to BARGE and BOURGAIN's in which pos. reactions were more often recorded. As far as "activity" is concerned, it is very difficult to compare two series, because a criterium to prove the similarity of two series in this respect is wanting.

As mentioned in the preamble it was as an indicator of the activity that BBR is expected to be of greatest importance from a surgical point of view. By operating in a most favourable phase of the disease, a direct spreading of the process may be avoided. DA SILVA's material included 4 cases with BBR+++ . In two of these cases no activity could be recorded clinically. Despite this, in one of the cases ureteral catheterization caused miliary tuberculosis, to a certain extent strongly reminiscent of CIBERT's cases, described earlier, of miliary tuberculosis due to a lesion of the urethra during cystoscopy; in the other case the continued course showed a distinct activity with a rapid development and spreading of the process. As to the other two cases, resection of the neck of the bladder was performed with a resultant tuberculous meningitis, in the fourth case no operation was performed. DA SILVA therefore suggests that surgical therapy should not be applied in those stages in which BBR is +++ or ++. Also in my material, as mentioned further up, a definite parallelism was discernible between pos. BBR and real activity, but in view of the risk possibly involved in an operation of a patient with strongly pos. or pos. BBR (+++ or ++), patients with urogenital tuberculosis were not operated on in these phases so that we have no personal experience of the danger of an operation during such periods. In three cases patients were operated on whilst in the weakly positive stage, all without complications.

As we however observed that operated cases which were neg. or weakly pos. before operation became pos. or strongly pos. the day after operation in no fewer than three cases, we henceforth avoided the performance of an operation as long as the patient reacted even BBR-weak. This change to pos. reaction after an operation with its manipulations seems to argue for the assumption that bacterial products and in all probability also bacteria are forced into the blood stream during an operation. Already earlier various authors (inter alia WILDBOLZ, MICHON, CIBERT) from different quarters have drawn attention to the possible risk of a spreading of the process at operation, and at the same time suggested many prophylactic measures. CIBERT also showed by experiments the possibility of a spreading of tuberculous material in renal tb. Now, if a pos. BBR already before the operation showed the passage of certain substances from the tuberculous process to the blood stream, the risk of a direct spreading of the infectious material at operation ought to be very great. It is of course not necessary for every "gush" of bacilli to involve a general spread of the process, the extent of the spread depending on various factors such as the size of the gush, patient's resistance etc. As there is a greater risk of the process spreading even if the patient is operated on in a weak BBR phase than in the negative phase we avoided surgical therapy and even cystoscopy at such times. If the possible liability of a spreading of the process can be diminished by a postponement of an operation, such postponement is warranted and indicated.

In this conjunction the timing of the active phase as registered by the BBR may be of certain interest. BARGE and BOURGAIN contend without however describing the course of the reaction, that the positive phase very quickly changes into negativity. As a rule we examined the patients for BBR within a couple of days after admittance, in one exceptional case it was somewhat later, but even then within 7 days. If the reaction was positive we repeated the test, if possible, until such times as the reaction had become negative. On some occasions we took as many as five tests of one and the same patient. In operated cases the BBR was tested 1—2 days after operation and if positive, we even then tried to follow up the patient until the BBR had become neg. The positive and strongly pos. reactions in urogenital cases generally became negative within 8—17 days after operation, the weak ones, after 4—5 days. In pulmonary tuberculosis the change to negativity



took more time, the strong reactions taking about 6 weeks, the weak ones, only about four weeks.

Examinations made in the follow-up of released patients showed that patients that had been discharged with a positive reaction became BBR neg. much slower than did those remaining at the hospital, and patients released with a neg. reaction have in some cases returned with a positive reaction again after a time, and then after a week's hospitalization again become negative. On the basis of the authors above mentioned examinations and after having perused material published earlier, it seems to me that cases in which the BBR is positive and thus tuberculous, and in all probability in the active phase, should be considered acutely ill and therefore confined to bed. The comparison of the duration of the active phase registered by the BBR in inmates and out-patients seems to argue for the importance of hospital nursing, offering rest and complete relaxation.

*Summary.* The results the author obtained, when clinically examining the reaction described by BARGE and BOURGAIN argue, especially in urogenital tuberculosis, direct for the correctness of the assumption that it is specific from a diagnostic point of view, only a pos. reaction however being of diagnostic value. By virtue of this specificity BBR should be very useful in diseases of suspected tuberculous nature, above all in the urogenital organs, especially in epididymitis and obscure hematuria.

The relatively short time necessary for the reading of a reaction renders possible an *early-diagnosis* in urogenital tuberculosis.

The parallelism apparently existent between BBR and the activity of the tuberculous process seems to be of certain value above all in determining the most suitable time to operate, it being observed that the patient should not be operated on as long as the reaction is positive. As a "phase indicator" however, it seems as if the reaction may become very important to the consideration of eventual treatment of tuberculous diseases.

As in-patients with positive reaction seem to give a neg. BBR quicker than out-patients, BBR-positive cases should presumably be hospitalized, thus assuring them of the necessary care, rest and relaxation.

The material published thus seems to furnish valuable information on a reaction which will in all probability become of great significance in the diagnosis as well as in the therapy of tuberculosis.

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## Potassium Metabolism in Connection with Operations.<sup>1</sup>

By

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During recent years increasing attention, especially on the part of American research workers, has been devoted to disturbances of the metabolism of the intracellular ions, particularly potassium, in various medical and surgical conditions. In "familial periodic paralysis" a fall of the serum potassium concentration has been shown to be the cause of the paralysis (1, 2). In diarrhea in children a large potassium loss has been demonstrated, which must be taken into account at the rehydration (7, 17, 18). In patients who have been aroused from diabetic coma by means of insulin and fluid treatment fatigue and paralyses have been found, caused by a fall of the serum potassium (20, 25). In renal disorders cardiac injury due to retention of potassium and elevation of serum potassium have been demonstrated (23); in other renal patients there has been increased loss of potassium with reduced serum potassium, fatigue, and paralyses (3). In adrenal disorders and Cushing's syndrome, too, disturbances in the potassium metabolism develop. A correction of disturbances of fluid and electrolyte metabolism as judged exclusively from a determination of the water balance and the extracellular ions is scarcely sufficient in all cases. However, this field is as yet far from fully elucidated, and so far it has not been possible to lay down clear principles for clinical use. The present study deals with potassium metabolism in direct connection with operations.

<sup>1</sup> This work has been aided by grants from Miss P. A. Brandt's Foundation.

## Remarks on the Pharmacology of Potassium.

Table 1 shows the concentration of some ions in the intracellular and extracellular fluids (6, 15). It is seen that the cells are very rich in  $K^+$ ,  $Mg^{++}$ , and  $HPO_4^{--}$ , whereas they do not contain  $Na^+$  and  $Cl^-$ ; this holds good especially of the cells in muscles, heart, liver, renal cortex, erythrocytes, etc., whereas the cells in connective and supporting tissues and spermatozoa are rich

Table 1.

*Concentration of Ions (mEq per Liter of Water) in Intracellular and Extracellular Fluid.*

Intracellular		Extracellular	
$Na^+$	0	$Na^+$	145
$Cl^-$	0	$Cl^-$	110
$K^+$	150	$K^+$	5
$Mg^{++}$	45	$HCO_3^-$	30
$HPO_4^{--}$	100		
$HCO_3^-$	12		

in  $Na^+$  and  $Cl^-$  (22). In the extracellular fluids (*i. e.*, the interstitial fluid and the blood plasma, which are of almost identical composition, apart from the fact that the latter contains more protein) especially  $Na^+$  and  $Cl^-$  are found, while there are but small amounts of  $K^+$ . There must be forces which normally keep these two groups of ions apart, the outer parts of the cell must be "impermeable" to these ions, whereas  $H_2O$  and  $HCO_3^-$  may pass freely. The normal serum potassium concentration is 3.7–5.1 mEq/l (14.5–20.0 mg%) (19).

Ordinary food is comparatively rich in potassium; milk contains approximately 140 mg%; a large helping of meat, potatoes, and spinach or cabbage contains approximately 2 g potassium. The intake of this amount by mouth causes only a slight elevation of serum potassium (21) (at most a couple of mg%) lasting a few hours; a far larger dose can be tolerated without intoxication; NORN (26) found by intake of 12 g KCl an elevation of serum potassium to 24 and 28 mg%.

An elevation of the serum potassium concentration to more than 10–12 mEq/l (39–47 mg%) is dangerous. Characteristic changes of the electrocardiogram, irregular action of the heart,

and cardiac arrest appear (7, 18). Such an increase will, however, be a rare occurrence; the organism will usually, even under greatly varying conditions, be able to keep the serum potassium concentration within normal limits.

Several times I have to moderately dehydrated patients administered by intravenous drip 600 mg  $K^+$  in 1,000 cc 5.5 % dextrose solution in the course of 2, 1½, or 1 hour; immediately afterwards the serum potassium concentration has in all cases been found to be normal, or only inconsiderably increased, maximum 5.6 mEq/l (21.8 mg%).

Ingested potassium is quickly deposited in the tissues and a surplus, if any, is later on excreted through the kidneys (10). By rapid injection of potassium-containing solutions the serum potassium may increase to such a degree that death occurs (27). Potassium intoxication is treated with intravenous injection of dextrose (deposit of glycogen is accompanied by deposit of potassium (14)) and  $Ca^{++}$  ( $Ca^{++}$  counteracts the effect of potassium on the heart (18)).

*Excretion of potassium* takes place, so to speak, exclusively through the urine; only in diarrhea the body is deprived of essential amounts in the stools (7). Even highly impaired kidneys can excrete potassium.

In a 49-year-old man (Case No 4241/47) with large bilateral renal calculi, pyonephrosis, and chronic uremia (blood urea 230 mg%, plasma bicarbonate 19 mEq/l), I found in a spontaneous diuresis of 4,500 cc an excretion of 1,580 mg  $K^+$  in 24 hours (he was on an ordinary diet) and a serum potassium of 5.4 mEq/l, *i. e.*, practically normal values. At autopsy four months later only very small renal remnants could be demonstrated.

However, also in serious renal disorders with reduced diuresis elevated serum potassium concentration with heart injury has been found (23), and in other chronic renal disorders potassium loss with lowered serum potassium (3), the latter condition manifesting itself with fatigue and paralyses.

If the renal function is entirely suppressed, or nearly so, in anuria or severe shock or dehydration, *e. g.*, following extensive burns, the serum potassium will generally increase, and in such circumstances it may be hazardous to give intravenous injections of potassium-containing solutions, even very slowly.

The potassium excreted in the urine may come from various sources:

- 1) It may originate from ingested potassium.

2) It may be liberated and excreted as a consequence of tissue breakdown; this excretion will run parallel to the excretion of nitrogen.

3) If the cells are damaged, *e. g.*, in anoxia, dehydration, or shock, the barriers of the cell frontiers will be broken, and  $K^+$ , and presumably other intracellular ions, escape from the cell (particularly muscles, heart, brain), and  $Na^+$  and  $Cl^-$  enter the cells;  $K^+$  is excreted in the urine. The passage of  $Na^+$  and  $Cl^-$  from the extracellular spaces (including blood plasma) into the cells may cause a reduction of  $Cl^-$  and  $HCO_3^-$  in the plasma (6, 7), *i. e.*, hypochloremia and acidosis will develop.

### Potassium Loss in Dehydration.

If the body is deprived of fluid, not only a water loss from the extracellular spaces occurs, but an essential part of the water loss takes place from the cells (11, 16, 30, 31), and at the same time some of the specially intracellular ions escape, and are at once excreted in the urine. A simply dehydrated patient will preeminently lose water and intracellular ions; the excretion of  $Na^+$  and  $Cl^+$  rapidly falls to nil (11, 16). In the first place, water and intracellular ions must be administered to such an organism; even if there is hypochloremia and low plasma bicarbonate, administration of isotonic sodium chloride and bicarbonate solution will fail to produce the desired effect, indeed, it will even increase the intracellular water and potassium loss (12). "*Physiologic sodium chloride solution*" is damaging to the simply dehydrated organism. If, on the other hand, a regular loss of extracellular ions has taken place, *e. g.*, by vomiting or aspiration of the stomach, such a loss must be replaced (4, 5, 13).

The serum potassium analyses made in this work have been carried out according to KRAMER and TISDALL's method as modified by CHR. N. J. GRAM (19) by precipitation of  $K^+$  as potassium sodium cobalt-nitrite and titration of this with potassium permanganate. The urinalyses have been performed after the same method after ashing in electrical oven. Control analyses and double analyses have shown the reliability of the methods.  $1 \text{ mEq/l} = 3.9 \text{ mg\% } K^+$ .

### Excretion of Potassium before Operation.

In 24 patients 30 determinations of the potassium excretion in the urine before the operation have been carried out. The

Table 2.

*K<sup>+</sup>-excretion in Urine, K<sup>+</sup>-concentration and Diureses Before Operation in 30 Patients.*

Period	K <sup>+</sup> -excretion	K <sup>+</sup> -concentration	Diureses
8—12..	80 mg per hour	235 mg per cent	38 ml per hour
12—18..	66       »	201       »	43       »
18—8...	54       »	192       »	33       »
24 hours	1,774 mg		872 ml

general condition of all the patients was good; they had been on an ordinary diet, and had not been dehydrated or had any metabolic disorders. The excretion has been calculated for three periods in 24 hours: 8 a. m.—noon (8—12), noon—6 p. m. (12—18), and 6 p. m.—8 a. m. (18—8), and is given in mg K<sup>+</sup> per hour. The average values of the potassium excretion, potassium concentration, and diuresis are shown in Table 2.

The potassium excretion is lowest during the night. The forenoon average is higher than that of the afternoon (in almost one half of the patients the opposite was, however, the case). The excretion per 24 hours was on an average 1.7 g; yet there was a very wide individual difference (variation 339—2,388 mg); since, as far as is known, the patients were in electrolyte balance, the variations in the excretion per 24 hours is presumably essentially due to differences in the potassium content of the food ingested; in some experiments this has actually been demonstrated. These variations per 24 hours correspond in all essentials to NORN's findings in experiments on himself (26). That the excretion is larger during the day than during the night can surely be explained by the potassium intake with the food; large forenoon excretion, in spite of a rather scanty morning meal, presumably indicate that a moderate dehydration has arisen during the night. The maximum potassium concentration measured was 426 and 402 mg%, all other values were less than 400 mg%. In 6 patients serum potassium was determined while they were fasting; it varied within normal limits 3.6—4.9 mEq/l (14.0—19.3 mg%).

### Potassium Excretion in Operated Patients.

In some patients the potassium excretion in the urine has been examined on the day of operation and on the following days.

An operated patient is exposed to several influences, which may all be assumed to affect the potassium excretion: the preoperative dose of morphine-scopolamine, the anesthesia, blood loss, operation trauma, and the greater or smaller reduction of the water or food intake following the operation. STEHLE, BOURNE, and BARBOUR (28) found in dog experiments lowered potassium excretion during ether anesthesia, but elevated excretion if morphine had been given previously; in all the experiments there was greater excretion during the 24 hours following the anesthesia than the day before; the series comprised only a few experiments. NORN (26) did not find constant conditions in rabbits. Blood loss is followed by increased excretion of potassium (29). In case of tissue damage (caused by a tourniquet) potassium is liberated from the cells (24). Dehydration and starvation will increase the excretion (11, 16, 30, 31).

#### Potassium Excretion in Operations without Parenteral Administration of Fluid.

Eight patients were operated under ether anesthesia, 3 of them on open mask, 5 under oxygen-ether anesthesia from anesthesia apparatus (the two different procedures did not make any difference in the potassium excretion); the operations were: 4 gynecological, 2 cholecystectomies, 1 tendon suture, and 1 extirpation of parotid tumour. The operations were carried out at 8 a. m., and one hour before the operation the usual dose of morphine-scopolamine (1 cg morphine hydrochloride and 0.4 mg scopolamine hydrobromide) was given. Blood loss was slight. No parenteral blood or fluid were given. During the first post-operative night 200—400 cc water was given by mouth, during the next 24 hours 800—1,700 cc water, oatmeal gruel, and milk with a total  $K^+$  content of 200—600 mg. The excretion of potassium and diuresis are shown in Table 3.

A comparison between Tables 2 and 3 shows: During the forenoon of the day of operation the potassium excretion is slightly reduced (preoperative average value in this group 89 mg/hr), but during the afternoon and night it is greatly increased. *The total potassium excretion during the 24 hours following the operation is greatly increased*, on an average 2,253 mg (variation 1,550—3,089 mg). In the following days the excretion falls to under preoperative value. The potassium concentration increases during the after-



Table 3.

*Average  $K^+$ -excretion,  $K^+$ -concentration and Diureses in 8 Operated Patients, Getting no Parenteral Fluid.*

	Period	$K^+$ -excretion	$K^+$ -concentration	Diureses
Day before operation		1,435 mg		974 ml
Day of operation....	8—12	63 mg per hour	209 mg per cent	36 ml per hour
	12—18	127 »	458 »	37 »
	18—8	85 »	429 »	19 »
	24 hours	2,253 mg		651 ml
2. day .....	8—12	65 mg per hour	280 mg per cent	24 ml per hour
	12—18	67 »	227 »	28 »
	18—8	35 »	214 »	16 »
	24 hours	1,008 mg		466 ml
3. day .....		700 mg		473 ml

noon and night following the operation (maximum 568 mg%). The diuresis is lower than before the operation corresponding to the slight ingestion of fluid.

In some of the patients analyses of serum potassium were performed. In all cases it was within normal limits; thus the increased excretion of potassium is not accompanied by any demonstrable increase of serum potassium.

Some of the factors which may be assumed to affect the potassium excretion have been examined separately:

In two experiments where a normal person had been placed on a standard diet for 72 hours it was not possible to demonstrate any effect of the subcutaneous administration of morphine-scopolamine on the potassium excretion, neither on the amount excreted per 24 hours, nor on the distribution over the various periods of the day and night.

On a normal person who had been on a standard diet for 72 hours a venesection was performed, in which 450 cc blood was withdrawn at 8 a. m. During the afternoon and night there was increased potassium excretion, so that the value during 24 hours was 25 % higher than in the three preceding 24-hour periods.

Two of the patients in Table 3 have undergone only minor operations, a tendon suture and an extirpation of a tumour in the parotid gland; they showed the same conditions as the others;

thus the extent of the operative intervention or tissue lesion is not of decisive importance for the increased potassium excretion.

It is not a specific effect of the ether anesthesia. Three patients operated on under spinal anesthesia (gynecological operations) had a potassium excretion of 2,424 mg during the 24 hours following operation; only 200—400 cc water had been given during the night. One of them showed the highest value found for the potassium concentration of the urine, 697 mg%, i. e., higher than the normal intracellular potassium concentration. During the preceding 24 hours the excretion had been only 1,477 mg on ordinary unrestricted diet. Four patients operated on under local anesthesia (3 hernias, 1 breast cancer) excreted during the 24 hours following operation 1,680 mg (during previous 24 hours 1,673 mg); here there was no increase of potassium excretion, but it remained constant in spite of no oral ingestion. Two normal experimental persons were subjected to the same limitation of fluid and food intake as the patients operated upon; the excretions during the 24 hours concerned were 1,768 and 2,143 mg K<sup>+</sup>.

*The potassium excretion during the 24 hours following operation exceeds to a great extent the amount released by tissue breakdown.* In 4 patients the nitrogen excretion was measured; from this the protein metabolism was calculated by multiplication by 6.3. Corresponding to the composition of the tissues not more than 15—20 mg K<sup>+</sup> can be liberated per gram of decomposed protein. The amount of potassium excreted during the 24 hours following the operation is twice as large as that which may be assumed to originate from decomposed protein. During the next 24 hours the potassium excretion roughly corresponds to the protein metabolism, the following days it is somewhat smaller.

*The increased excretion of potassium during the 24 hours following operation must thus be due to water loss from the cells.* This will occur if an amount of fluid not large enough to replace that lost by insensible water loss and diuresis is given; glycogen mobilization from the liver due to starvation will cause an escape of water and potassium from the liver cells (14); blood loss, if any, will likewise induce a cellular dehydration accompanied by escape of potassium. When the excretion has not been so high in patients in local anesthesia, or in persons only subjected to a limitation of the food and fluid intake, this is presumably due to the fact that the dehydration in such cases is not so pronounced as in more extensive surgical procedures under general or spinal anesthesia.

Table 4.

*Average  $K^+$ -excretion,  $K^+$ -concentration and Diureses in 5 Operated Patients, Getting Adequate Parenteral Fluid Therapy.*

	Period	$K^+$ -excretion	$K^+$ -concentration	Diureses
Day of operation ...	8—12	38 mg per hour	107 mg per cent	50 ml per hour
	12—18	70 »	222 »	34 »
	18—8	43 »	165 »	30 »
	24 hours	1,184 mg		819 ml
2. day .....	8—12	51 mg per hour	90 mg per cent	126 ml per hour
	12—18	44 »	54 »	128 »
	18—8	22 »	43 »	75 »
	24 hours	782 mg		2,323 ml
3. day .....		192 mg		1,490 ml

#### Potassium Excretion in Operations with Adequate Parenteral Fluid Administration.

According to the foregoing one should expect to find an essentially lower excretion of potassium in patients, to whom adequate amounts of fluid have been administered after the operation. The average for five patients of this category appears from Table 4. The patients underwent operations on the stomach, colon, or biliary tract. During the 24 hours following the operation 1,200—4,000 cc of 5.5 % dextrose solution was given intravenously; in two of the patients blood transfusions of 500 and 1,000 cc respectively were given. During the next 24-hour period 2,000—3,000 cc of dextrose solution was administered. *The potassium excretion during the 24 hours following operation was only half as large as in the patients who received no parenteral fluid; in none of them it exceeded that which might be assumed to originate from tissue breakdown.* During the following days the potassium excretion decreased further, the great diuresis at the same time suggesting a certain overhydration of the organism. Maximum potassium concentration in the urine measured was 347 mg %.

Two patients operated under local anesthesia for hernia had during the day of operation drunk and eaten as usual; the excretion on the day of operation did not vary from that of the days preceding and following operation.

### Discussion.

Thus in connection with operations an increased potassium excretion is found. This applies especially to the first postoperative afternoon where the dehydration begins to make itself felt, less so during the night where the water loss, on the whole, is smaller, cf. the lower diuresis. During the following days, as a rule, the excretion does not exceed that which may be assumed to originate from tissue breakdown. The increased potassium excretion is due to the development of cellular dehydration, since it is not found in case that adequate amounts of fluid are administered.

The experiments show that as soon as a water deficiency in the organism arises, fluid is taken both from the intracellular and extracellular water stores to replace insensible water loss and diuresis. The intracellular water loss is not very large. A loss of 2,000 mg  $K^+$  corresponds to a loss of intracellular water of approximately 400 cc (Table 1); this corresponds to  $\frac{1}{2}$ — $\frac{1}{3}$  of the water deficiency to which the organism has been exposed during the 24 hours following operation.

These conditions may further support (in addition to the shock prophylaxis and other harmful effects of dehydration) the view that any surgical patient should be treated with adequate volumes of blood and fluid. The best fluid to use is a 5.5 % dextrose solution if there is no pronounced loss of certain electrolytes.

Some investigators have warned against *transfusions of bank blood* owing to the potassium content of the plasma. The potassium content will increase when bank blood is stored, even though there is no hemolysis of the blood cells. DE GOWIN, HARRIS, and PLASS (8) have in blood stored for a fortnight found a serum potassium concentration of approximately 140 mg%, in blood stored for 30 days approximately 170 mg%. I have analysed 4 portions of bank blood (after shaking), which had been stored for varying lengths of time. The potassium analyses of the plasma (double determinations) are shown in Table 5. It is seen that there is no risk that 500 cc bank blood, within the first 2—3 weeks, should contain more than approximately 250 mg  $K^+$  in the plasma. There is no risk involved in using it for transfusion, cf. that 600 mg  $K^+$  has been given intravenously in 1 hour without essential increase of serum potassium. Only if many transfusions are to be given in quick succession, or in case of renal insufficiency,

it is advisable to prefer fresh blood. DE GOWIN, HARDIN, and HARRIS (9) transfused blood with a serum potassium concentration of up to 150 mg% at a rate of 40 cc per minute, and did not find any changes of the electrocardiogram or essential elevations of serum potassium (maximum 2.4 mg%).

Table 5.  
*K<sup>+</sup>-concentration in Plasma of Bank Blood after 2-20 Days Storage.*

	Days storage	Hemolysis	K <sup>+</sup> -concentration mg per cent
1.....	2	none	42.3
2.....	4	none	74.7
3.....	12	moderate	75.1
4.....	20	slight	89.0

A routine administration of potassium after all operations is not indicated if only an adequate amount of fluid is given. I have done it occasionally, but the potassium administered was excreted as a surplus. If, on the other hand, potassium is administered 1-2 days after an operation in which an adequate amount of fluid had not been given, some of it is retained, which may be taken as an expression of an existing potassium deficit. The serum potassium concentration will not increase.

If, on the other hand, for some reason or other a pronounced dehydration is present, it is indicated to add K<sup>+</sup> to the intravenous fluid; we have done this in the solution used by BUTLER, which also contains other intracellular ions:

Sodium lactate .....	2.24 grams
Potassium chloride .....	0.89 »
Potassium phosphate (dibasic) .....	0.25 »
Sodium chloride .....	0.58 »
Distilled water .....	50.0 »

One ampul is mixed with 1 litre of 5.5 % dextrose water and given as intravenous drip in the course of some hours. Each ampul contains 600 mg K<sup>+</sup>; 4-5 portions may be administered daily as required.

Although it is outside the scope of this work, a brief report will be given by way of illustration:

K. J. (Case No 2709/48) underwent an abdomino-perineal rectum amputation under spinal anesthesia. Blood and dextrose water were given permanently as intravenous drip. During the first four post-operative days a total of 9,806 mg  $K^+$  was excreted; diuresis was lowered. On the third postoperative day a paralysis of the stomach developed, and permanent aspiration was instituted. During the following days the above-mentioned  $K^+$ -containing solution (2—4 ampuls daily) was given in dextrose water and saline. The potassium excretion fell, and the potassium administered was retained. Not until after 6 days was the potassium balance restored. At that time 10,200 mg  $K^+$  had been given, and only 2,781 mg excreted. Thus during the first postoperative days there was a large uncompensated loss of potassium; whether or not this had been an instrumental cause of his gastric paralysis is impossible to say.

A rational potassium therapy is unfortunately difficult to establish so far owing to the lack of a quick method of analysis, which can be employed as a routine in any laboratory.

### Summary.

There is an increasing understanding of the significance of disturbances of the metabolism of the intracellular ions in various medical and surgical conditions. Among the intracellular ions potassium is present in the highest concentration. Certain points of the normal potassium metabolism is mentioned.

The potassium excretion on an ordinary diet is on an average 1,700 mg per 24 hours, varying from approximately 400 to approximately 2,400 mg. The excretion is lowest in the night, generally a little greater in the forenoon than in the afternoon.

Surgical patients to whom no parenteral fluid has been administered have greatly increased potassium excretion during the 24 hours following operation, especially during the afternoon. This increase is due to cellular dehydration on account of the negative water balance. If adequate amounts of fluid are administered, the potassium excretion does not exceed that which corresponds to the tissue breakdown.

Routine administration of  $K^+$  after operation is not necessary if only adequate amounts of fluid are given.

If, on the other hand, the organism is dehydrated, it is indicated to add  $K^+$  to the intravenous fluid. By way of illustration a case is reported in which 10 grams  $K^+$  had to be given before the potassium balance was attained. Our experiences with potassium treatment will be published later.

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## Retropubic Prevesical Prostatectomy.

By

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Retropubic prevesical prostatectomy is no new method, as stated in TERENCE MILLIN's article in "The Lancet" in 1945.

The method has first been described in 1909 by the Dutch author W. J. VAN STOCKUM. Through a medial incision he entered the prevesical space of Retzius, and reached the anterior surface of the prostate gland. The veins were ligated and the adenomae enucleated through a longitudinal incision of the prostatic capsule. A tampon was placed in the prostatic cavity and the bladder drained through a small slit in the vesical roof. The wound was then closed around the tampon and the drain, both of which were removed 5th day after the operation. At this time a catheter was placed in urethra and left in site until the wound was dry, about 12th day. The author believes that vesical drainage through urethra the whole time, without an extra opening into the bladder, would be equally effective. His results were good, but the method never became much used.

A similar method was accounted for in 1924 by the German author OTTO MAIER. He made an incision into the groin above Poupart's ligament, working his way to the lateral surface of the prostate. The veins were ligated and the prostatic capsule opened through a longitudinal incision of its lateral surface. After enucleation of the adenomae the capsule was sutured and bladder drainage instituted through a urethral catheter, left in for about 8 days. The abdominal wound was primarily closed around a small drain, which was allowed to remain for a few days. Also Maier's results were good and his method recommended.



The same method was since 1927 used by the Swedish surgeon VICTOR HENRIKSON, who, instead of an lateral approach, used a median to the anterior surface of the prostate.

In 1933 retropubic prevesical prostatectomy was described in detail by the American surgeons JACOBS & CASPER. They used medial incision above the symphysis. Otherwise their technique shows no essential difference from that of Maier. They tried, however, to conserve the posterior part of urethra.

According to W. K. IRWIN, a method similar to the one used by Millin, has been described by the Italian authors CARRARO & WUGMEISTER in 1938 in their book on prostatic hypertrophy.

The advantages offered by the retropubic prevesical prostatectomy are several. The method must be regarded as an anatomically natural one, offering an extravesical approach to the extravesical organ of the prostatic gland. The transvesical route seems rather irrational, demanding two separate openings into the bladder for the approach to an organ situated outside the bladder. — Besides, the retropubic prevesical approach to the prostate is the shortest one. The method is sparing, implying no lesion to other organs. A full view of the prostatic cavity is gained, and hemorrhages are completely controlled. Also the post-operative treatment is very simple and comfortable for patient and nurses. The patient is soon out of bed, a condition that very likely will reduce the frequency of thrombosis and embolism. These are experiences common to all who have used the method.

The method is preferably used for adenomatous prostates, but is probably capable of application to all types of prostatic obstructions. I have used the retropubic prevesical approach by complete removal of prostate in 3 cases of early carcinoma, with good result. This method by early carcinoma of the prostatic gland is also proposed by VICTOR HENRIKSON and later by H. S. SOUTTAR.

The essential arguments carried against the retropubic prevesical prostatectomy is the limited space behind the symphysis that renders the operation a difficult one. Next there is the danger of fistular formation, the stiff anterior wall of the cave of Retzius — the symphysis — tending to impede a rapid closure of the space. Additionally comes the risk of major hemorrhages from the extensive plexus of veins surrounding the prostate and bladder.

These objections may seem just, with the present method, however, we believe to have solved these difficulties.



Fig. 2. The puboprostatic venous plexus after injection of contrast into the deep dorsal vein of the penis.

MATHISEN: Retropubic Prevesical Prostatectomy.



Fig. 7. Urethrography. Prostatic cavity 12 days after removal of goos-egg-sized adenoma. (85 gms.)

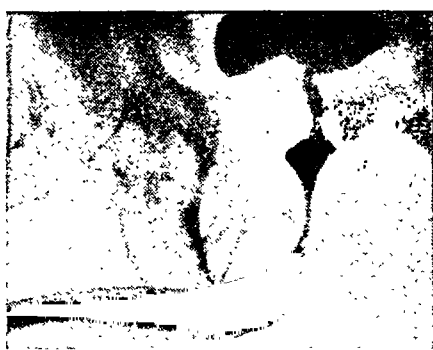


Fig. 8. Urethrography. Same patient 3 months after operation.



Fig. 9. Urethrography. One month after complete removal of prostate early carcinoma.

MATHISEN: Retropubic Prevesical Prostatectomy.

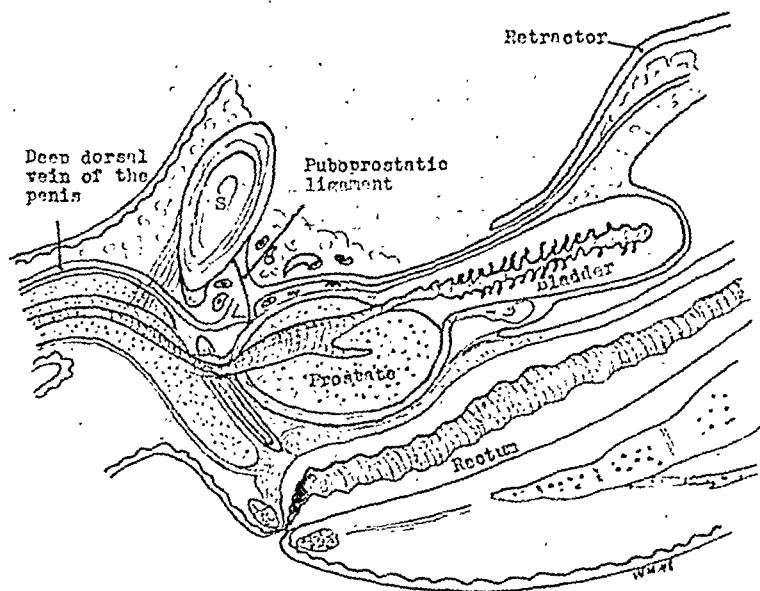


Fig. 1. Section of the prevesical space of Retzius.  
(See also Fig. 4.)

The use of the method requires a thorough knowledge of the anatomical conditions, specially of the prevesical space of Retzius. The most important features will therefore be defined.

*The space of Retzius:* When the bladder is carried upward, the prevesical fatty tissue, containing a few veins is brought into view. Ligation of these veins and retraction of the fatty tissue exposes the prostate gland covered by a thin sheath.

Under this sheath a number of veins are seen running obliquely across and to the sides of the prostate, arriving from the inferior side of symphysis. These veins form part of the pubo-prostatic plexus. Near the prostatic apex the sheath continues into the lower part of the symphysis, forming the rather dense pubo-prostatic ligaments, the most important distal fixation of the prostate. Less important are the loose fibres from the prostatic capsule downward to the urogenital diaphragma. Section of the pubo-prostatic ligaments and the prostatic fascia to both sides and digital detachment of the tissue around the prostatic apex possibilizes an upward mobilization of the prostate of 1—2 cm, on a level with the symphysis. This is an important condition that essentially facilitates an approach to the prostate.

The veins of the pubo-prostatic venous plexus are situated under the thin prostatic sheath on the anterior and lateral aspects

of the prostatic surface. This venous plexus is chiefly supplied from the deep dorsal vein of the penis. There are also communications with vesical and rectal veins. Ligation of the deep dorsal vein of the penis in close proximity to the symphysis essentially controls hemorrhages from the anterior part of the venous plexus.

*Preoperative treatment.* — Most patients arrive with considerable, often complete retention, and most with reduced renal function. The preoperative treatment for all follows the usual lines: the bladder is drained through a urethral catheter, and vasectomy is at once performed under local anesthesia. Acidosis is treated with bicarbonate, normal fluid balance restored etc. Intravenous urography is made when blood urea has fallen below 50 mg. %. Electrocardiogram is taken before the operation.

According to Millin should drainage of the bladder be avoided in order to prevent preoperative infection. Just before commencing the operation, however, he introduces a cystoscope and places a catheter in urethra, both procedures naturally infect the bladder and thus the operative field. To avoid an infection the catheter must be inserted from above during the operation and cystoscopy omitted.

As for infection of the bladder from drainage, in our experience as that of many others, this has no injurious effect, but acts rather like an autovaccination — a favourable one. The longest drained and most infected cases often progress the most smoothly.

Before the operation the patient is out of bed for a couple of days. For removal of mucous etc. the bladder is thoroughly irrigated before the operation. Sulfanilamide is given one day before and 3—4 days after the operation.

*Operative technique.* — The operation is performed under spinal anesthesia. To obtain a more vertical approach to cave of Retzius a pillow is placed under lumbar region of the patient, this increasing lumbar lordosis and tilting the pelvis to a more vertical position of the symphysis. — When placing the patient in Trendelenburg position an eventual bleeding will diminish. — A thin Nelaton's catheter is installed in urethra and the bladder emptied. This catheter must be so thin as to fit into the tube to be used for vesical drainage, and that is slipped into the urethra from above in course of the operation. For bringing the prostate gland closer to the surface after section of the pubo-prostatic ligaments a rubber bulb mounted on a thick catheter is used. Capacity of the rubber bulb is about 200 cc. After greasing with vaselin the

bulb is placed in the rectum ampule before beginning of the operation. Connection with an irrigator can filled with water is established, so as to permit filling and emptying of the bulb as desired. This is particularly useful during enucleation of the adenomae and during suturing.

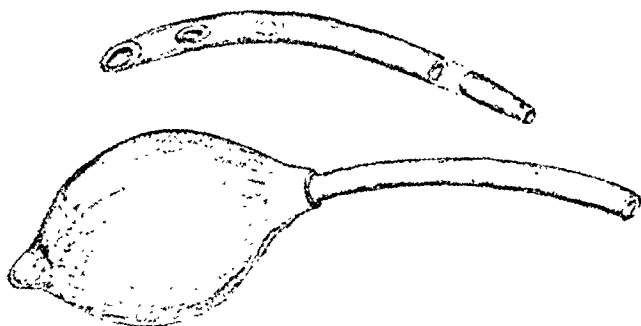


Fig. 3. Rubber tube for vesical drainage through uretra, and rectal rubber bulb.

The abdominal incision is made from radix penis to a distance from umbilicus. At site of the attachment of sheath and muscles to symphysis the incision is continued about 1 cm to either side to facilitate the survey. Before proceeding with the operation the deep dorsal vein of the penis is ligated proximate to the symphysis. Because of the position of the vein under the penile fascia, section and subsequent suturing of the lig. suspensorium penis may be necessary.

The bladder is carried upward and held in position by means of a retractor. The musculature is retracted with a self-retaining speculum. The light must be good, and the operational field preferably illuminated by a small lamp hanging down behind the symphysis, or fixed on the retractor. The veins of the prevesical fatty tissue are ligated and the fatty tissue kept to the sides of the prostate with serviettes. After removal of the fat from the anterior prostatic surface the pubo-prostatic ligaments are dissected transversely close to the symphysis with a diathermy knife, and the prostatic fascia severed on both sides. The veins on the anterior prostatic surface are underrun with the boomerang-needle and ligated, whereafter the capsule is incised longitudinally from the neck of the bladder to the prostatic apex, down to the adenomae — using the diathermy knife.

The capsule is loosened somewhat to the sides and enucleation of the adenomae can be performed, the bulb in rectum first being filled with water.

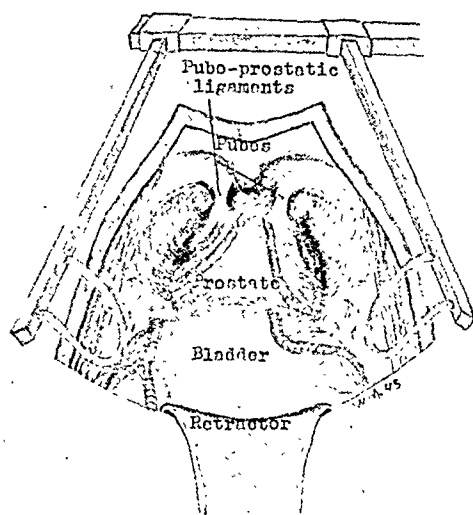


Fig. 4. The prevesical space of Retzius. The veins of the puboprostatic venous plexus are situated on anterior and lateral aspect of the prostatic surface, under the fascia.

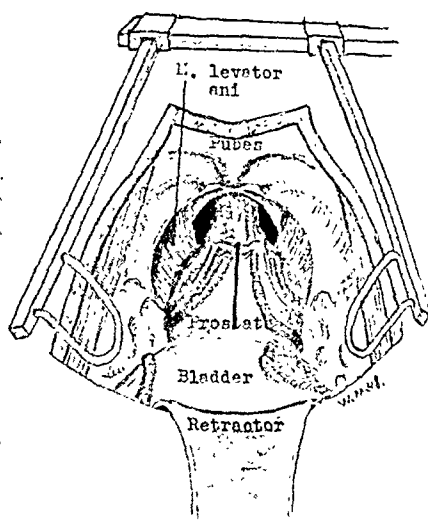


Fig. 5. The puboprostatic ligaments are divided and the prostatic fascia severed, permitting upward mobilization of the prostate. Incision in the prostatic capsule is marked.

Enucleation is started from the side and down toward the apex, then up toward neck of bladder. In the presence of several fair-sized adenomae, these are removed separately to prevent tearing of the capsule. Upward the adenomae are fixed to the vesical mucous membrane and are here dissected with the diathermy knife. A compress is temporarily placed in the prostatic cavity and the vesical opening caught with 3—4 curved Kocher clamps and bleeding spots coagulated. The compress is removed from the prostatic cavity and bleeding spots coagulated. During these manipulations the catheter in urethra has been tucked aside.<sup>1</sup> When hemostasis is satisfactory, the catheter is inserted into one end of the tube that is to serve for vesical drainage and fastened with a silk thread suture. Drain and catheter are greased with oil and pulled through urethra. The drain tube should be 60 cm long and with an internal diameter of about 5—6 mm. It ought not be too soft to prevent kinking. About 5 cm should be left inside the vesical opening. On the sides of the drain perforations are made 1.5 and 3 cm from the tip. — Diameter of the urethra is about 8 mm approximately corresponding to the external

<sup>1</sup> 3 Harris-sutures are placed through the posterior lip of the vesical neck and the prostatic capsule. This will stop bleeding from the prostatic arteries, and prevent secondary hemorrhage.

diameter of the drainage tube. — After installation of the drain the prostatic cavity is packed with a piece of "Gelfoam" saturated with saline solution, "Coagulene" or best of all with plasmathrombin. This will control remaining minor hemorrhages. The "Gelfoam"-piece must be great enough to fill the prostatic cavity.

As for "Gelfoam", reference is made to directions following the preparation.

The prostatic capsule is sutured in two layers with continuous catgut sutures. Distally the boomerang-needle is used for suturing the capsule. The sutured border is covered with the prevesical fatty tissue that contributes to fill out of the cave of Retzius. A small drain is left in and the wound closed in layers.



Fig. 6. Catheter-belt in site.

The vesical drainage tube through urethra must be well fixed, either with sutures to the inferior side of penis or by means of a special catheter-belt, that we have found very useful, the sutures often cutting through allowing the catheter to slip out. The catheter-belt is seen in Fig. 6.

The belt is applied outside the dressing, that consists of a compress, an absorbent pad and protected by oil silk.

Incision of the prostatic capsule has been partly transverse, partly longitudinal. The longitudinal incision is, in my experience, beyond comparison the best. It follows the direction of the vessels, gives a good survey of the entire prostatic cavity, and is easiest one sutured. Leakage is rare connection with the longitudinal incision, whereas after transverse incision it has been frequent complication.

When doing complete removal of prostate in cases of early carcinoma, the operation follows the same route. After dividing



the pubo-prostatic ligaments and prostatic fascia, the prostate is caught with a clamp and drawing upward. The urethra carrying the catheter will be palpable and then divided at the apex of the prostate. The prostate is shelled out from the fascia of Dénon villiers, which separates the prostate from the rectum. With a diathermy knife the prostate is detached from the bladder, beginning at the anterior surface of the bladder neck, to both sides and backward, dividing the ejaculatory ducts. After having ligated all bleeding points, the vesical drain is passed through the urethra and into the bladder. Anastomosis of the bladder with the membranous urethra is then made. There remains then a portion of the bladder still to be closed, and closure is effected by continuous catgut in the median line. The bladder is now sutured to the triangular ligament and to the levator muscles, obliterating the bed of the prostate. The bladder-drainage remains about 14 days.

*Postoperative treatment.* — The cigaret drain is removed from the wound 2nd day and the patient allowed up 3d—4th day. The urethral catheter is removed 8th—10th day when there is no leakage of urine into the wound. In this case the catheter is left to remain until the wound has been dry for 2—3 days.

Bladder irrigations have not been used as postoperative treatment. If drainage is poor the catheter is changed. Change of catheter before 5th—6th day is difficult, and has not been necessary since the introduction of large drainage tubes instead of catheter that easily become closed up. Also has the catheter-belt prevented the drainage tube from slipping out.

*Results.* — 40 patients with benign prostatic hypertrophy, aged 59 to 85 years, averagely 69 years, have been treated. Preoperative drainage of the bladder has been carried on from 1 to 9 weeks. Postoperative drainage from 8 to 23 days. Leakage of urine occurred in 9 cases. For these cases transverse incision of the prostatic capsule had preferably been used. The last 14 cases operated according to the above method have had no leakage of urine. In 2 cases hypertrophied lobes were present in conjunction with carcinoma. In one of these recurrence and stricture of the internal orifice developed 2 months after the operation. Otherwise there has been no stricture nor distressing infection of the prostatic cavity. One patient with hypertonia died 5th day after the operation of pneumonia.

The size of the enucleated adenomae has been from 30 to 105 gms.

Postoperative hospitalization has been averagely 17 days, as a rule 12—14 days. Observation period has been 2 years.

The prostatic cavity shows comparatively rapid involution. 3—4 months after the operation — or sooner — mere traces are demonstrable in urethrography.

### Summary.

Retropubic prevesical prostatectomy has been described in 1909 by the Dutch author W. J. VAN STOCKUM, and later, with various modifications, by others. The method has earlier not been much used.

A description is given of the most important anatomical features of the space of Retzius, the venous plexus and lower fixation of the prostate to the symphysis being specially mentioned. The operative method is described, and a number of modifications mentioned.

40 patients have been operated, of whom 1 died of pneumonia the 5th day after the operation. Leakage of urine has occurred in 9 cases and lasted from 5—8 days. Average postoperative hospitalization has been 17 days, as a rule 12—14 days.

The method is recommended as the most natural route for prostatectomy, with low mortality and few complications. The same route is also recommended by complete removal of prostate in early carcinoma.

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## **A Case of Habitual Posterior Subluxation of the Shoulder Joint Operated According to Clairmont-Ehrlich.**

By

HANS EKMAN.

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In recent years two cases of habitual posterior subluxation and luxation respectively have been published in Scandinavian literature. The dislocations occurred backward in the shoulder joint during elevation and inward rotation (SJÖVALL and MÖLLERUD). The term habitual has been used here in its narrower but stricter sense to indicate a luxation, which always occurs in a joint when, during a movement, the joint-surfaces have acquired a certain position in regard to each other. This type has sometimes been referred to as pendular luxation (REISCHAUER). In Scandinavian and German periodicals especially, the term "habitual" is also employed for the dislocations which usually appear in the form of a typical traumatic displacement and recur at longer or shorter intervals, more or less "spontaneously". This is less adequate, however, and contributes towards terminologic confusion. In respect to this last mentioned group, however, the term "habitual" should be replaced with the more exact indication "recurrent" (SJÖVALL, REISCHAUER). SJÖVALL proposes that a general classification of all the luxations be made on the basis of BLUMENSAAT's system regarding the patellar luxations. In this way, an improved and more uniform terminology would be achieved in this domain. But obviously, even BLUMENSAAT's classification would not serve to remove all the terminologic difficulties when more complicated cases exist, which are not easy to place schematically.

We have recently had a case at the surgical department I of Sahlgrenska sjukhuset for the treatment of double-sided habitual posterior subluxation in the shoulder joints.

The patient was a female student 19 years of age. Case report 1021/46. (<sup>20</sup>/<sub>3</sub>—<sup>10</sup>/<sub>1</sub> 1946.)

No earlier known trauma. Keen gymnast in her school-days. Practised leap-frog diligently. No gymnastics the last 3—4 years owing to discomfort in the right shoulder joint. On several occasions during the elevation forward-upward of the right arm, had noticed *clickings in the right shoulder joint, a jerk backward, and inability to continue the elevation*. When the arm was lowered, the clickings recurred and the arm could be moved in the ordinary manner. Since the autumn of 1945 these discomforts have considerably increased and last month the condition was unbearable. The clickings in the right shoulder joint and the incapacity to move the arm, now occurred with every greater elevation.

Moreover, on several occasions, the right arm luxated more severely, especially when shaking hands, shaking carpets, playing tennis, thus, in the performance of elevations forward-upward, of a rougher kind. As a rule, the arm shall then have pointed forward and downward. When this occurred the patient was obliged to seek help in order to coax the arm right again. No medical aid was resorted to however. The arm was kept bandaged some days. During recent months the right arm sometimes luxated while the patient slept. It then lay upwards and behind the neck. Of late, the arm was bandaged during sleep to prevent dislocation. *Similar, but less pronounced discomfort also begun to make itself felt in the left shoulder joint.*

Admitted to the surgical department <sup>20</sup>/<sub>3</sub> 1946. Moderate atrophy of the musculature in the right shoulder region. When the right arm is in elevation forward-upward or forward-outward, *a subluxation always occurs in the right shoulder joint* at an elevation of about 60—70 degrees. This is facilitated by a simultaneous slight inward rotation. Palpation gives convincing evidence that the head of the humerus lies posteriorly. When the head slid backwards the same clicking sounds were observed by the patient. Reference might be made in this connection to the discussion between KARPIS and MATHEIS on this phenomena, and the explanation of the same (*Schulterschnappen*, snapping shoulder). Elevation above the horizontal plane is impossible, due to the previous subluxation which the patient is unable to prevent voluntarily. Even if the arm be held alongside the body, an inward rotary movement and jerk backwards can displace the right humerus head backwards. When this occurs, it appears to be mainly the pectoralis major and anterior part of the deltoid muscles which enter into function. Elevation of the arm also produces backward subluxation of the humeral head *on the left side*, but this is less pronounced and less constant, however.

X-ray examination on <sup>20</sup>/<sub>3</sub> 1946 reveals that the subluxations on both sides occur backwards.

In accordance with the terminology of BLUMENSAAT and SJÖVALL, the case should be practically characterized as habitual, bilateral posterior subluxation in the shoulder joints. Sometimes with more violent movements there also occurred posterior luxations in the right shoulder joint. To simplify matters these might also be apprehended as a severer type of the habitual backward subluxation.

It is undoubtedly not a case of purely voluntary subluxation since it occurred during sleep and since it could not voluntarily be prevented by the patient.

By reason of the acute discomfort in our case an operation was performed.

*27/3 1946. Operation performed on the right side, according to the Clairmont-Ehrlich method (Op.: the author).* The operative procedure was carried out conformably with the description published in *Der Chirurg* 8: 276: 1936. Dissection of the lateral shoulder interval. From the posterior incision it is possible to detach the posterior fourth of the deltoid from the humerus without disturbing the nerve and vessel supply to the deltoid. The posterior part of the capsule appears to be somewhat wide and is drawn together with a few stitches. The posterior fourth of the deltoid is drawn forward through the lateral shoulder space and attached to the anterior rim of the deltoid. The arm is then fixed in plaster thoracobrachially, at an elevation of about 80°.

Apart from a slight infection in the anterior wound the postoperative course was good. The patient was discharged from the hospital on Ap. 10, for ambulant treatment. The plaster was removed on Ap. 23, and physical therapy followed. The patient was able to return to work (office work) on May 9.

*Reexamination 28/10 1946.* No recurrence of luxation or subluxation in the right shoulder joint since the operation. The right shoulder joint shows decrease in muscular power of elevation outward-upward and forward-upward to about  $\frac{1}{4}$ — $\frac{1}{3}$  as compared with the left. Right, elevation: forward-upward 150°, outward-upward 150° and backward-upward 40°. (Actively = passively.) Left, elevation: forward-upward 170°, outward-upward 170° and backward-upward 50°. Rotation at 90° elevation in the right shoulder joint 100° and in the left 180°. (Actively = passively.) All these movements were performed with the cooperation of the scapula. Constant subluxations in the left shoulder joint, but so far, these give very little trouble. The operative results hitherto are very satisfactory.

*Reexamination, 12/6 1948.* More than two years have elapsed since the operation. Neither luxation nor subluxation has occurred in daytime. On awakening in the morning the patient has occasionally found the right arm in a peculiar position. With a slight jerk the arm can be easily moved. The sensation was not similar to that in the event of the earlier subluxations. The force of the right arm is somewhat dimin-

ished but is capable of performing all the more usual activities. The patient can participate in lighter sport, paddling for instance, without difficulty, but still avoids elevations of the right arm which require special effort such as in tennis. The discomfort of the left shoulder joint has considerably increased. *Status*: The right arm is elevated outward-upward and forward-upward without subluxation backwards. The movement of the right shoulder joint is almost normal but there is a slight reduction of muscular power. On the other hand, however, with every elevation forward-upward, there occurs a subluxation backwards in the left shoulder joint before the arm reaches the horizontal plane, and the anterior part of the deltoid especially, as well as the pectoralis major are involved. The outward-upward elevation is performed without subluxation. The patient is very satisfied with the results of the operation even though there is some feeling of uncertainty in regard to the right shoulder joint. The discomfort arising from the left shoulder joint has increased, but is not so great that she deems an operation necessary at present.

It thus seems that within the group of posterior shoulder joint dislocations are rather rare but none the less important group might be included which, widely seen, is characterized by a constantly occurring subluxation or backward displacement of the humeral head during the performance of an elevation or inward rotation of the arm. The luxation often occurs just at a combination of these two movements. In the event of lowering or outward rotation the arm reverts to its normal condition. Although the luxation occurs at a certain point during the performance of an active movement, it may not be characterized as voluntary, when the patient is unable to prevent the dislocation at this phase of the movement. It can even be induced passively against the patient's will. The term habitual (SJÖVALL, BLUMENSAAT) should be appropriate for this group of posterior, permanent, involuntary luxations. To draw a line of demarcation between the latter group and the group of posterior luxations which occur at longer or shorter intervals, more or less "spontaneously", in other words, recurrent luxations, should not be difficult as a rule. If the definition of a voluntary luxation is clear (MATHEIS), *i. e.* if reference is made to a dislocation and reposition occurring under the influence of the will (accompanied by strain or the relaxation of certain muscles) which cannot be induced passively against the patient's will, and whose occurrence the person in question can always prevent, the delimitation between the habitual and voluntary luxations is not difficult to accomplish in the typical cases.

In severe neurologic diseases, syringomyelia, sclerosis en plaques, poliomyelitis, and certain arthritic disturbances, similar posterior displacements sometimes occur (pathologic luxations). They are of little interest, however, in this connection.

Accordingly, besides the fresh, traumatic posterior shoulder joint luxations, the recurrent, habitual and voluntary dislocations are also be classified in main groups. On the other hand, there can also be cases of a more complicated nature which are exclusive of these groups but which might be said to be combination-cases like ASPLUND's case of voluntary and involuntary recurrent luxation. Such cases may be described as they are, and this need not involve effacement of the limits between the main groups.

Besides the published cases of SJÖVALL and MÖLLERUD, there are reports in the literature of a number of posterior habitual shoulder joint luxations in their narrower meaning. GULEKE and KAPLAN have each described a case of a boy 15 years of age and a girl of 17 respectively. HINDENACH's case was a man 24 years of age with a habitual posterior luxation which had developed from a traumatic shoulder joint injury. In the one case of REISCHAUER, a girl 7 years old had bilateral habitual displacement of the humeral head backward-downward. SEIFERT's case referred to a man aged 47 years with a left-sided luxation, which was at first traumatic, but afterwards developed into habitual luxation. KAISER and SEIFERT have pronounced their cases as voluntary, but they would seem preferably to belong to the habitual. They cannot possibly be included among the voluntary solely because the dislocation occurs in a certain position during the performance of an active phase of movement, if the criteria for a voluntary luxation are otherwise not fulfilled.

The cases published by HOHMANN and OMBRÉDANNE reporting congenital shoulder luxations revealed aplasia of the humeral head and the joint surface of the scapula, but were otherwise very reminiscent of the habitual dislocations. FÈVRE and MIALARET also reported a case of posterior habitual humeral luxation in an aplastic shoulder-region of a girl 11 years old. These cases approach more nearly the pathologic luxations however.

While including his own case and those of SJÖVALL and MÖLLERUD in the group of habitual luxations, the writer would wish to assign to the same, the cases of GULEKE, KAPLAN, KAISER, HINDENACH, REISCHAUER and SEIFERT. On going through the liter-

ature of recent years the impression is given that a further number of solitary cases of this form of displacement exist, but as the descriptions are incomplete, the writer has not gone any further into them. Such were three cases of HENDERSON with posterior capsuloraphy, and the cases of BUSCH, HUNTLEY, LINHARDT, SCHINZ, TEICHER, VOLKMANN, ROWE and YEE and others. Some of the cases which are reported as voluntary, including those published by BERTHEIN and KOCH, are described in such a manner that now, maybe, one is unable to determine with accuracy whether these were cases of real voluntary luxations or whether or not they should have been characterized as habitual.

As the discomfort to which these patients are subjected is generally severe, operation is often the ultimate. In GULEKE's case mention is made of the use of a fascial strip, analogous with Kirschner's plastic. KAISER employed a combination of a Kirschner plastic and the insertion of a bone-graft at the posterior glenoid rim. In the cases of HOHMANN, FÈVRE-MIALARET, HINDENACH and OMBRÉDANNE a posterior bone-support was constructed, in doing which OMBRÉDANNE used a graft from the spina scapulae. Finally, the Clairmont-Ehrlich operative method was employed by SJÖVALL and the author, while KAPLAN reversed the Clairmont technique. He conveyed a piece of the anterior deltoid through the quadrilateral space and fixed it posteriorly. As vessels and nerves enter into the posterior part of the deltoid muscle it should be very difficult — in the event of KAPLAN's operative method — to supply an anterior part of the same with vessels and nerves, in other words, to secure a functioning muscle. The good operative results reported in this case (well after 3½ years) would possibly seem due to the anterior part of the deltoid being put entirely out of action. The cases of MÖLLERUD, SEIFERT and REISCHAUER were not operated. The observation periods after operation are rather short in the published cases. For this reason, and owing to the paucity of the cases, it is not possible to come to any greater conclusions with reference to the most suitable operative methods. The most expedient would seem to be the insertion of a bone-graft at the posterior glenoid rim or an operation according to Clairmont-Ehrlich. It would not seem out of place in this connection to touch upon the results of the Clairmont-Ehrlich operation. It is not so highly esteemed nowadays in respect to the anterior luxations, on account of the relatively high recurrence frequency. ANSCHÜTZ re-



ports 12 cases with 6 recurrences and KUSMIN 34 cases with 8. Personally, and from English literature HOBART has collected 43 cases with 14 recurrences. (This includes RYERSON with 10 successful cases and HENDERSON with 8 and 4 failures.) Some of these collocations give no information as to whether anterior or posterior luxations are concerned but probably they refer wholly or exclusively to the former.

The purpose of the Clairmont-Ehrlich operation was to create a muscular sling on the inside of the humeral neck. This muscle would contract when abduction occurred, and prevent an eventual anterior displacement. In the opinion of Clairmont and Ehrlich the head of the humerus was supposed to dislocate inferiorly in abduction. There is a high percentage of recurrences with the Clairmont-Ehrlich operation in anterior shoulder luxations. It is easy to understand this, as MOSELEY says, when the view that the head displaces forward rather than straight downwards is accepted.

When after the Clairmont-Ehrlich operation the muscular sling lies firmly fixed on the medial side and a part of the posterior humeral neck, but is less stable forward-downward, the numerous recurrences in respect of the anterior humeral luxations are easily understood. In many instances the portion of the deltoid which was moved, undoubtedly and partially degenerates, although the vessels and nerves have been spared as far as possible (OETIKER, HENDERSON). MANDL found this muscular sling in a degenerated state when reoperating a patient who had already undergone the Clairmont-Ehrlich operation. WATSON-JONES is of the opinion that the effect is due more to the cicatricial formation. This will occur more extensively on the posterior and interior of the *collum chirurgicum*.

From this is apparent that the effect of the Clairmont-Ehrlich operation must be considerably more favourable in regard to posterior than to anterior luxations. MANDL, for instance, warmly recommends the Clairmont-Ehrlich technique for the posterior luxations. As operated cases of posterior humeral dislocation are rather few, it is obviously difficult to know which operation is preferable. The Clairmont-Ehrlich method employed in the posterior luxations, as seen in the cases of SJÖVALL and the writer, yields however satisfactory results without any greater impairment of the muscular force or mobility of the shoulder joint. It might thus well be employed for the habitual posterior luxations

when the operation is indicated by reason of the involved discomfort which is generally very severe.

### Summary.

The writer describes a case of double-sided, posterior, habitual subluxation in the shoulder joint of a young woman. Owing to excessive discomfort an operation according to Clairmont-Ehrlich was performed on the right side. Reexamination on the elapse of two years after the operation showed good results. In connection with the same, the terminology in regard to luxations is discussed with special reference to SJÖVALL and BLUMENSAAT. The term habitual is employed in its more limited sense. An account is rendered of cases of posterior, habitual humeral luxation reported in the literature.

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## The Operative Treatment of Female "Stress" Incontinence.

By

HERMAN WAHREN, M. D.

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Urinary incontinence in women can be the result of widely divergent causes. Neurogenic disturbances, congenital or acquired fistulas etc. may be present. This study is only concerned with the involuntary escape of urine through the intact urethra in connection with sneezing, coughing or other types of muscular strain. To this type of incontinence the word "stress" is often applied, the cause being the sudden increase of the intraabdominal pressure.

There exists up to this day a considerable degree of confusion and incongruity in perineopelvic anatomy. Some authors consider *e. g.* the sphincter urethrae membranacea and the deep transverse perineal muscle as separate entities, whilst others believe them to be one and the same formation. The external voluntary sphincter appears under various names such as sphincter urethrae membranacea, sphincter urogenitalis, "the muscle of micturition" (KENNEDY) etc. Also the functionally highly important fascia surrounding the bladder are described with extremely great variation. Great difficulties are caused to descriptive anatomy owing to the fact that so many different formations containing smooth musculature and hard to differentiate meet round the neck of the bladder. Besides there should be great differences between the pelveo-perineal musculature of virgins and multigravidae. An acceptable, detailed exposition of the anatomy of the bladder and urethrae with an analysis of the differences in various authors would occupy too much space and is beyond the scope of this paper. There are works by CURTIS, ANSON and

ASHLEY and also KENNEDY treating these problems. Even if a detailed exposition of the kind is impossible the author should like to draw a quick outline of the clinically important aspects of the anatomy of the bladder and urethrae as follows: The bladder and the urethra are surrounded by the general pelvic fascia. Especially strong musculo-tendinous elements fix the perineo-urethral tissue under the surface of the symphysis pubis. The three muscular layers of the bladder are continued round the urethra. Round the neck of the bladder these layers thicken and differentiate and are known as the internal urethral sphincter or the lisso-sphincter (MARTIUS). A separate group of these fibers is often called *musculus trigonalis*. These fasciculi originate at the back of the neck of the bladder between the urethral orifices. They continue subsequently parallelly to the urethra giving rise to folds in the mucosa. Beyond the latter there is a layer of cavernous tissue (*corpus spongiosum urethrae*). These folds and this cavernous tissue are most probably of a certain significance to urination. The incontinence troubles often vary according to the menstrual cycle and the blood supply to the abdominal organs. Where the urethra pierces the floor of the pelvis cross striated muscle-elements are connected to the wall from the levator ani, bulbo- and ischiocavernosus as well as from the diaphragma urogenitale (*sphincter urethrae externus*).

The levator ani is of extremely high importance to the problem of incontinence. This mighty muscle gives the bladder support against the pressure of the abdominal musculature and against the varying pressure conditions in the abdominal cavity. By vaginal palpation the two fasciculi of the muscle can easily be felt, they are often called *ligamentae pubo-coccygeae*. In nulliparae the distance between these ligaments is about 3 cm but it is increased considerably after parturition.

The physiological emptying of the bladder is dependent on the intimate interplay between nervous and muscular factors. *Also the position of the neck of the bladder is highly important to which more and more attention has been paid by authors of late years.* Disturbances of various kinds both in the muscular function and in the position of the bladder can give rise to incontinence.

As has been said before the trauma of parturition plays an important rôle in "stress incontinence". TAYLOR and WATT have shown that the majority of women with such incontinence have borne children and that the symptoms increase with the number

of births. How then does parturition influence the urinary apparatus? Earlier authors, ZANGEMEISTER, MACHENRODT, TAYLOR and WATT etc. supposed that tearings or distensions arose in the muscular sphincters after parturition. But nowhere can any proof be found that this supposition is correct. On the other hand it is quite natural that the pelvic floor with the levator ani is subjected to intense strains during parturition, and that the fasciculi of the levator (the ligamenta pubo-coccygea) are distended, relaxed and forced apart. Thus the muscular support of the bladder is decreased. The lowering of the neck of the bladder can easily be the result. WATSON also considers himself to have established that the parturition trauma causes, besides injuries to the levator musculature, a distension of the musculo-tendinous fascia which extends from the symphysis to and round the neck of the bladder. The same opinion is expressed by KENNEDY (1947).

A highly interesting investigation of the bladder-emptying mechanism has been carried out by S. KARLSON. With extremely delicate apparatus he has been able to establish that urination can be provoked when urine enters the posterior urethra. Thereby a reflectory contraction of the detrusor musculature in the bladder is provoked. It is conceivable, although by no means proved, that when the muscular support of the bladder decreases and its position with regard to the symphysis is lowered, urine may enter more easily into the posterior urethra than under normal conditions and thus cause vesicular contraction.

*Operative treatment of "Stress Incontinence".* Previous operative methods reflect the opinion formerly held by clinicians that the incontinence was due to insufficiency in the urethral sphincters. GERSUNY tried torsion of the urethra often with a deleterious effect. The same author subsequently attempted to compress the urethra by injecting paraffine but only with a temporary effect. The best known and still often used method is KELLY's shortening of the internal sphincter with mattress sutures. In this country ÅKERBERG has used a modification of the method with raphi from cavum Retzii. Other, more complicated methods where it is tried to substitute the effect of the sphincters with muscular force from other sources are GOEBELL's pyramidalis plastics of which there are many modifications and also GIORDANO-DEMINGS gracilis plastics. Other muscles or groups of muscles have also been used for the same purpose.

In modern literature the interest has been moved away from the muscular sphincters proper, and more attention is being paid to the position of the neck of the bladder in relation to the symphysis and the changes in the surrounding muscles and fascia resulting from parturition. As soon as these principles had been generally accepted, the therapeutic results improved considerably.

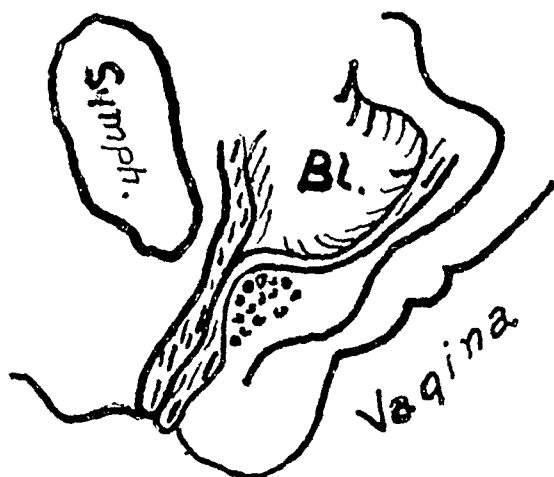
In order to raise and support the bladder NATVIG has performed interposing of the uterus according to SCHAUTA (in anglo-american literature this operation is known as WATSON transposition operation). MARTIUS has worked out a plastic operation in which the musc. bulbo-cavernosus with the surrounding adipose tissue is laid free and inserted under the neck of the bladder. FRANK has achieved an elevation of the fundus of the bladder by using the anterior portion of the levator ani. The latter method has been further developed by INGELMAN-SUNDBERG, who also moves the orifice of the urethra nearer the clitoris. He reports excellent results by this method. FRANK, KENNEDY and WETTERDAL describe principally similar raphae of the fundus and neck of the bladder.

*The author's own material and experience.* My interest in the treatment of "stress incontinence" dates from the reading of ÅKERBERG's work in 1940. I operated my four first cases according to KELLY's original method. All four cases relapsed within 18 months. In two cases the operation was repeated with the use of ÅKERBERG's modification; no permanent result was achieved. Two cases were operated upon according to GOEBELL with a pyramidalis plastics. In one of the latter cases SÜNDE's modification was used. Both cases relapsed within a short time. Two more cases were operated upon with the use of MARTIUS's bulbo-cavernosus plastics. One of them was successful but in the other one necrosis arose with infection of the transplanted material. As it is difficult, at least in some cases, to procure sufficient nutrition for the inserted adipose muscle flap, this method can hardly be recommended.

The only operation that has given a lasting result was therefore the bulbocavernosus plastics which fairly effectively elevates the neck of the bladder. A much more reliable elevation of the neck of the bladder and a more effective constriction of the space between the sides of the levator is achieved by the transposition of the uterus, so that the fundus uteri supports the anterior part of the bladder. Seven operations of this kind have been per-

formed.<sup>1</sup> The observation period for these cases ranges from 6 months to 4 years.

There is only one drawback to this operation, which was first used for incontinence by NATVIG, *i. e.* it can not be applied in all cases. It is contra-indicated for women in the fertile ages, it can



not be used where the uterus is enlarged and it is difficult to perform technically when the vagina is narrow.

In order to achieve an elevation of the neck of the bladder and a support for the fundus with the slightest possible trauma, I have through incision in the anterior fornix grafted bone-chips from the tibia behind the neck of the bladder between the cervix uteri and the wall of the bladder. (See the figure.)

*Technique:* Portio is drawn down by forceps. A small transverse incision is made in the anterior fornix and the posterior wall of the bladder is laid free from the cervix uteri so that a piriform space is shaped behind the neck of the bladder. The drawn portio is covered by a compress and without contamination 5—7 cc bonechips are inserted. The bone tissue can conveniently be taken through a small osteotomy on the medial side of the upper part of the tibia. The material should for the greater part consist of cancellous bone which combines better in healing with the soft parts than the cortical chips. The material can easily be excised with a spoon.

It can be mentioned in this connection that if the transposition of the uterus is used as incontinence-operation the fundus uteri should be well fixed under the symphysis *e. g.* by means of sutures

<sup>1</sup> One of these operations has been performed by Dr G. SUNDELIN, Gyn. Klin. Eskilstuna Hospital.



through the anterior part of the lig. pubo-coccygea. Sometimes it is difficult totally to cover the fundus uteri with vaginal mucous membrane, which did not, however, in my cases entail any complications.

In the first few cases I used os purum (ORELL) as supportive material behind the neck of the bladder, bone-chips are however more easily assimilated. This method has been used for the operation of seven cases with excellent result. In one case a post-operative bronchitis and trombosis arose and after some time the transplanted material was infected and had to be removed in part. But the final result was still satisfactory. In one of the os purum-cases a breakthrough of the os purum-material to the vagina took place about half a year after the operation. The observation period for these cases ranges from 7 months to three years.

*Conclusion.* "Stress incontinence" is due to a change in the position of the neck of the bladder relative to the symphysis and to changes in the musculature surrounding the bladder particularly the levator ani, rather than to insufficiency in the sphincter musculature. Therefore the position of the fundus and the neck of the bladder should be restored and supported.

### Summary.

It is the experience of the author that the best method in cases of stress incontinence is the transposition of the uterus. In cases where this method is contra-indicated good results have been achieved by the grafting of bone-chips from the tibia between the cervix uteri and the neck of the bladder.

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## Perirenal Abscess.

By

OLA OBRANT.

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Thirty-two cases of perirenal abscess (PA) have been operated upon at the Surgical Department I, Sahlgrenska Sjukhuset between 1920—1945. The operation consisted of incision and drainage in all cases, in only one case pyelostomy was also performed. Thus the material has been treated in an equal manner.

The chief purpose of this report is to establish the results of the operative treatment by a subsequent examination of the cases, and to investigate if the kidney may show any sequelae of a perirenal abscess; furthermore to consider in what manner the results of this investigation might induce any alterations in the treatment of the disease.

It was earlier believed that a suppuration can primarily occur in the perinephrium, the so called “*périnéphrite idiopatique*” (RAYER 1839 etc.). At present however it is considered (COUVELAIRE and others) that PA is practically always secondary either to staphylococcal infection of the kidney parenchyma (pyonephritis) or to an infection in the renal pelvis and parenchyma (pyelonephritis).

In the former case it can be a question either of a diffuse suppuration in the kidney or of a limited focus which sometimes is even healed at the time of the diagnosis of PA.

In those cases where pyelonephritis was the cause of a PA the kidney has often shown severe pathological changes (COUVELAIRE) *e. g.* a pyonephrosis with or without a calculus, etc.

According to the above the cases have been divided into two groups:

I. Abscessus perirenalis pyonephriticus (PA PYO): 18 cases, 13 men and 5 women.

II. Abscessus perirenalis pyelonephriticus (PA PYEL): 14 cases, 9 men and 5 women.

The average age of the patients at the beginning of the illness was with PA PYO 35 years and with PA PYEL 54 years. These figures are higher than the usually stated ones, depending upon the fact that Sahlgrenska sjukhuset does not receive patients under 16 years of age.

The abscess appeared on the right side in 17 patients, on the left side in 14 and one was bilateral. In the group PA PYO there were nine right and eight left sided and one bilateral infection, while in the group PA PYEL the abscess was in eight cases right-sided and in six cases left-sided. The predominance of the dextral location is often more marked, such as in FRANZAS' data with 66 right-sided and 34 left-sided abscesses.

The average interval between the date of admission to the surgical ward and operation was 20 days, the shortest interim was zero days and the longest was two months and 19 days. The date of inception of the symptoms was determined in 31 cases with a mean interval from inception to operation of five weeks. R. J. DOUGLAS has reported a mean of 23 days for the corresponding interval while FOWLER and DORMAN give a mean of 7.5 weeks, which illustrates the diagnostic difficulty of this disease.

The average time from operation to discharge was in the PA PYO group one month and three days, in the PA PYEL division two months and 21 days.

The bacteria causing the abscesses have been examined in 22 cases by a cultivation from the pus obtained by incision (Table 1). In the PA PYO group only staphylococci appeared while the PA PYEL division exhibited different strains.

The localization of the abscesses in regard to the kidney is reported in 13 cases as follows: two were superior, one was lateral and superior, three were posterior and inferior and seven were inferior. The literature gives the most common localization as posterior, this is probably because of the static condition of the patients for they are early confined to bed by the disease. The same conditions have been observed by H. EKMAN in cases of perirenal spontaneous haematoma.

PA symptoms are extremely abundant. The most consistent symptoms are pains and aches which were absent in only one case belonging to the PA PYEL group. The symptom of pain in

Table 1.

*The causative bacteria found by cultures of the pus.*

## I. Abscessus perirenalis pyonephriticus.

Case No.	1	6	10	11	12	13	14	15	17	18	20	21	22	25	26	28	29	30
Staphyloc. albus .....				+	+	+	+						+					
Staphyloc. aureus .....			+					+	+	+					+			+
Staphyloc. not grouped ...											+			+		+	+	+
Cases not examined .....	+	+										+						

## II. Abscessus perirenalis pyelonephriticus.

Case No.	2	3	4	5	7	8	9	16	19	23	24	27	32
Staphyloc. albus .....								+					
Staphyloc. not grouped .....											+	+	
Streptococ. anhaemolytic .....													+
Streptococ. mucos. ....					+								
Gram-positive diplococcus .....										+			
E. coli .....						+							
Cases not examined .....	+	+	+	+			+		+				

this group is of little significance for the diagnosis of PA, because the primary disease itself may cause the pains as in renal calculi. Therefore only pains occurring in the PA PYO group are discussed. The pains were localized as follows: Renal area and lumbar region, 5 cases; abdomen, 8 cases; legs and hip joints, 3 cases and buttock region, 1 case. The nature and intensity of the pains have varied quite considerably, usually it has been reported as a continuous and dull pain.

Symptoms of "a severe cold", coughing and stitch in the side

The results of the laboratory tests of the urine.  
I. Abscessus perirenalis pyonephriticus.

Pat. No.	1	6	10	11	12	13	14	15	17	18	20	21	22	25	26	28	29	30
Albumin .....																		
Pus in sediment .....																		
Staphylococcus .....	2	2																
Coli and paracoli .....																		
Proteus .....																		

II. Abscessus perirenalis pyelonephriticus.

Pat. No.	2	3	4	5	7	8	9	16	19	23	24	27	31	32
Albumin .....														
Pus in sediment .....														
Staphylococcus .....	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Coli and paracoli .....														

<sup>1</sup> Double-sided PA with a nephritic picture and great numbers of red blood corpuscles in the sediment.  
<sup>2</sup> Urine from the affected side obtained by catheter.  
Pus in sediment: — = In some cases no white blood corpuscles, in others only single ones. ++ = Rich in white blood corpuscles.

were observed in 10 patients, seven in the PA PYO group and three in the PA PYEL division. In five cases of the PA PYO group the diagnosis of pleuritis was made at the beginning based upon X-ray and puncture findings.

Gastrointestinal symptoms are most often reported when the abscess is anterior to the kidney, appendicitis and cholecystitis are then often simulated. Two patients, one from each group, had a primary appendicectomy. In both cases the appendix was entirely normal. In two other cases a laparotomy was at first performed because of suspected gall-bladder affection.

One patient with PA PYO who had been admitted to an infectious diseases' hospital for suspected typhoid fever was later transferred to the surgical ward when the bacteriological tests proved to be negative.

Cystitis symptoms occurred infrequently. Within the PA PYO group only one case suffered from slight frequency.

In the PA PYEL group urinary troubles and frequency occurred in three patients. Further more in one case a cystostomy had been made because of prostatic hypertrophy and in two patients urethral strictures were found.

The results of the laboratory tests of the urine are given in Table 2. In the PA PYEL group pus and bacteria could be found in every case. In the PA PYO division pus was not seen in any of the sediments, eight of the cases showed bacteria in the urine.

Table 3.  
*Leucocytosis in 25 cases of PA.*

White blood corpuscles/mm <sup>3</sup>	Number of patients	
	PA PYO	PA PYEL
6—10 thousand.....	4	3
11—15 " .....	5	2
16—20 " .....	3	2
more than 20 thousand ...	2	4

Leucocytosis is common in PA but not in any way constant. Twenty-five patients were examined, the results are given in Table 3. These figures refer to the highest value established in each case. The maximum was 37 thousand. Four PA PYO and

three PA PYEL cases did not show any value higher than ten thousand.

A NPN (non-protein nitrogen) test taken during the first few days of 18 cases showed in 14 a value under 40 mg %, four of which were PA PYO and 10 were PA PYEL. A value of over 40 mg% was found in two patients from each group, 46 and 111 mg% respectively in the PA PYO, and 47 and 44 mg% in the PA PYEL division.

The case with a NPN of 111 mg% died while at the hospital. The post-mortem examination showed cystopyelonephritis apostem. NPN had decreased to 44 mg % following the operation.

Fever has been considered to be the most consistent symptom in PA but not less than three patients have been afebrile. The majority have been febrile usually with high continuity but other forms of fever have occurred.

Sedimentation Rate (SR) was tested in 27 patients on admission. Two of the afebrile cases had an SR of 103 and 120 respectively. The figures listed in Table 4 show that extremely high values were found in both groups.

Tab. 4.

*Sedimentation rate on admission.*

S. R. in mm/1 hr	No. of cases	
	PA PYO	PA PYEL
0—20 .....	0	0
21—40 .....	0	2
41—60 .....	1	2
61—80 .....	3	3
81—100 .....	4	3
101—120 .....	4	3
121—140 .....	2	0

An extremely important symptom in PA is the palpable resistance in the loin, that in this survey could be found in 11 cases in the PA PYO group, with fluctuation in two, and in the PA PYEL division in nine cases with fluctuation in three.



The roentgenological possibilities for confirming the diagnosis of PA have been described in detail by SKARBY (1946). Only the frequency of the positive X-ray findings in the 30 patients who were examined in this way will be given here (Table 5). At the time of the X-ray examination the fixation of the kidney has not been noted.

In ATCHESON's study of 117 cases, extending over about the same period of time as this survey, there were non-pathological findings in 55 per cent of the cases through roentgen examination.

For differential diagnosis between PA PYO and PA PYEL the history and the urine findings are of very great value, the urography is particularly decisive.

In the case of PA PYO it is therapeutically important to ascertain if the PA is secondary to a kidney carbuncle which sometimes produces conspicuous alterations in the pyelogram (first described by LJUNGGREN in 1931).

In the case of PA PYEL it is essential for the purpose of planning the operation to establish the existence of any other disease within the kidney or urinary system, where it is particularly important that there is no obstruction.

As in this survey there are several patients who were examined more than 20 years ago, many of the cases have not been examined with modern methods. Thus urography has not been used in several of them.

In the PA PYEL group the following complications have been noted:

Calculi in 6 cases (5 of which in X-ray examin.)

Pyonephrosis in 3, perhaps 4 cases

Infected hydronephrosis in 1 case

Pyelonephritis in 4 cases, one of which showed purulent liquefaction of the kidney.

### Treatment.

RAYER had already stated in 1839 that PA should be incised. This form of therapy has prevailed since that time. The question whether the operation should be extended to more than a simple incision however has been the subject of discussion.

Relatively little consideration has been given to the influence of chemotherapy upon PA. Most of the patients in this survey were treated prior to the use of chemotherapy, only two cases

Table 5. Roentgen Findings.

Table 5. Roentgen Findings.																																
Case No.	PA PYO																PA PYEL															
	1	6	10	11	12	13	14	15	17	18	20	21	22	25	26	28	29	30	2	3	4	5	7	8	9	16	19	23	24	27	31	32
Method of examination	u	p	p	r	r	p	p	u	r	u	p	r	r	r	0	r	r	r	r	u	r	u	u	u	u	p	u	p	p	r	u	0
Obliteration of psoas shadow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Obliteration of kidney shadow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Visible mass in the loin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Enlarged kidney shadow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Renal cavities due to purulent liquefaction	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Displacement of kidney and ureter	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Kidney pelvis and calyces deformed	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Dilatation of kidney pelvis and calyces	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
No excretion at intravenous urography	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stone shadows	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Displacement of colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Concavity of spine to side of abscess	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Diaphragm not moving on side of abscess	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
No pathological findings	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Case No.	1	6	10	11	12	13	14	15	17	18	20	21	22	25	26	28	29	30	2	3	4	5	7	8	9	16	19	23	24	27	31	32
u = intravenous urography, p = retrograde pyelography, r = plain roentgenogram.																																

received sulfa preparations, one prontosil and the other sulfa-thiazole. Both were without effect and both cases had a fatal outcome. Penicillin has not been administered to any patient.

### Re-examination.

Fourteen of the 32 patients died while 18 are living at present. I have re-examined 16 of the living patients and two have been contacted by questionnaire.

Interval between operation

and re-examination:	5 years	10—14	15—19	20—25
No. of pats. with PA PYO ...	—	6	5	3
No. of pats. with PA PYEL..	1	2	1	—

A physical examination has been made of the heart, lungs and abdomen. The blood pressure has been measured and the urine examined with reference to albumin and sediment with a bacterial culture made from the sediment; NPN was determined and urography performed.

The roentgen examination has been of particular interest and in all cases this was made in the form of an intravenous urography. The shadow of the earlier affected kidney has been visible on the radiograph except in two patients. One of these is a fistual case and will be described later and the other showed only indistinct superior boundaries and otherwise nothing abnormal.

Ever since 1907 it has been known that the renal mobility in the PA side at respiration is less than that of the non-diseased side. I thought it interesting to study the permanency of this fixation.

Table 6.

*Roentgen examination of the mobility of the kidneys with patient in different positions made at the re-examination several years after the operation.*

Case No.		PA PYO						PA PYEL
		6	11	20	21	22	28	9
Movement shown in heights of vertebrae	PA side	$\frac{1}{2}$	$\frac{1}{2}$	0	$\frac{1}{3}$	0	00	$\frac{1}{2}$
	Non-diseased side	2	$1\frac{1}{2}$	$\frac{1}{2}$	1	1	—	2

In the re-examination the renal fixation has been investigated with the patients in different positions (Table 6). The normal displacement when changing from a prone to an erect position should be 4—5 cm according to HILGENFELDT (as reported by SKARBY). The displacement is somewhat greater in women than in men and slightly greater on the left side than on the right side.

In one PA PYEL and six PA PYO cases there were a total or a relative fixation of the earlier diseased kidney. In six cases the examination revealed nothing remarkable and in three patients these details were not noted during the urography.

The blood pressure showed nothing notable (Table 7).

Table 7.

*Systolic blood pressure at re-examination.*

Blood pressure (mm Hg)		225	220	180—165	150—135
No. of patients . . . . .	PA PYO	—	1	6	6
	PA PYEL	1	—	2	—

### The PA PYO group.

Of the 18 PA PYO cases 14 are living. Thirteen of them were examined and one replied to a questionnaire.

All were subjectively well at the time of the re-examination.

Albumin in the urine occurred in one patient without any further positive findings.

Two patients had slightly increased NPN (about 50 mg%), and pus cells and bacteria in the urine. Radiography showed in one of them a fixation of the earlier operated kidney, the other kidney was conspicuously mobile and hydronephrotic. Roentgen examination of the other patient, who was the only bilateral case, showed the left kidney to be normal while the right kidney pelvis and calyces were slightly deformed. The calyces were compressed with irregular contours and the neck of the calyx leading to the lower group was narrowed. "The deformation was conditioned by an inflammatory shrinking". Upon a position change both kidneys proved to be fixed.

NPN was normal in the other patients.

Of the four *deceased patients* in this group two died while being treated in the hospital for PA.

No. 25. Died 10 days after the operation from bronchopneumonia.

No. 14. Died 53 days after the operation. The autopsy of this case showed bilateral cystopyelonephritis apostematosa and purulent liquefactions in the lungs. (This case has been classified as PA PYO since the infection probably secondarily spread from the kidney parenchyma over the urinary system. Urine proved to be sterile immediately preceding the operation.)

No. 1. Died one year after operation from an acute peritonitis due to an enteritis with paradysentery four months earlier. The autopsy showed nothing notable about the kidney.

No. 29. Died 17 years after the operation in pulmonary tuberculosis.

### The PA PYEL group.

Of the 14 cases with PA PYEL only four are now living and two of these four have fistulae.

One of these cases was operated upon 11 years ago (No. 8). Urography before the operation showed no excretion from the affected kidney and also revealed several renal calculi. Following the operation a fistula remained but this fistula was closed for several short periods, and then the patient constantly showed high fever and chills which ceased when secretion was resumed.

On urography at re-examination there was no excretion in this kidney and no renal shadow was to be seen. An almond-sized dense calcium shadow that was believed to be a urinary concretion was seen. By a contrast filling of the fistula a cavity was found just below the skin from which a bifurcated fistula duct emerged, one fork that lead towards the kidney region, showed a contrast defect corresponding to the described stone shadow.

The patient's NPN was 46 mg%. Urine: no albumin, in the sediment pus and coli. The secretion from the fistula was purulent, a cultivation of the bacteria exhibited enterococci.

The other patient who had a post-operative fistula for the last five years (No. 3) and where roentgen examination immediately after the operation showed a coral stone on the affected side, has stated in a letter that the wound was healed about five months after the operation and remained closed for approximately three months. Thereafter a fistula appeared in the scar and this has since been present with purulent secretions. Urination difficulties in the form of a burning sensation and frequency have occasionally occurred.

The third living patient is subjectively quite well. There is trace of albumin in the urine, the sediment exhibits modest quantities

of pus cells and is rich with coli. Urography revealed bilateral moderately dilated kidney pelves and ureters. NPN was 22 mg%.

The fourth patient was finally operated upon in 1935, at which time a concretion in the right ureter was revealed by roentgen examination. This stone was voided in June 1936. Since then the patient has not had any urinary troubles. At the re-examination the urine sediment showed solitary white blood corpuscles and coli bacteria. The urograph is now normal, except the fixation of the kidney on the operated side.

There are ten *deceased patients* in this group.

No. 5. Died seven days after operation. The incision for PA was combined with a pyelostomy, but a stone in the ureter was left behind. This stone was found at autopsy to be impacted 5 cm. below the kidney pelvis. Both kidneys presented a picture of "pyonephrosis apostematosa" at the post-mortem examination.

No. 4. Died 11 days after operation. The post-mortem examination showed bilateral pyonephrosis and a perforation from the abscess into the duodenum.

No. 32. Died 12 days after operation. Autopsy showed an impacted ureteral stone 5 cm. above the linea anonyma, the ureter was dilated above the stone and contained pus. A perforation through the posterior wall led to the abscess. In addition was found a pyelonephritis, an acute peritonitis, pneumonia and duodenal ulcer.

No. 16. Died one month after operation. Autopsy showed PA and pronounced kidney changes in addition to a prostatic abscess and a septic thrombus in the heart, a septic infarct in the spleen and purulent peritonitis.

No. 7. Died five months after operation. The patient at the time of operation was 71 years old and a year earlier had had a bladder fistula for hypertrophic prostate. No autopsy was performed.

No. 19. Died 11 months following operation. The cause of death was cancer ventriculi. No autopsy was made.

No. 2. Died one year and 5 months after operation in calculus renis permagn. sin. cum pyelitis et fistula. No autopsy was performed. X-ray examination preceding the incision showed several large stones in the kidney pelvis.

No. 27. Died two years after operation. Death was from a crural abscess on the same side as the PA. Autopsy showed the right kidney to be strongly fixed to the surrounding tissues. The kidney showed no alterations.

No. 23. Died two years and three months after operation in bronchopneumonia and acute bronchitis.

No. 24. Died nine years following operation. A fistula remained until the patient's death, the cause of which was a hematemesis from a stomach ulcer. Retrograde pyelography two months after the incision showed hydronephrosis. No autopsy was made.

There has been a remarkable difference in the results of the operative treatment between the abscesses developing from the pyo- or the pyelonephritis. In the PA PYO-division four cases out of 18 have died, two of these from a disease unrelated to the previous PA. In association with the operation one patient died from sepsis and one from bronchopneumonia. Otherwise the patients are living and all are free from symptoms. Objectively it has been possible to indicate a renal fixation in six of the patients and a deformation of the kidney pelvis in one of these cases. The operation, incision and drainage of the abscess has thus proved to be fully satisfactory to effect a healing. There were no carbuncles of the kidney, that could be demonstrated as a basis for PA in any of the cases. In such cases the general opinion in the literature is that the operation should be enlarged, *e. g.* with an enucleation of the carbuncle.

It is an entirely different situation in the PA PYEL group that is partly due to the difference in age between the two groups. In the PA PYEL division 10 out of 14 patients have died, six as a direct result of PA and four of these in association with the operation. Two of the cases that died at a later date had fistulae persisting until their death. Of the four now living two have fistulae, one patient had coli-pyelitis and bilateral dilated kidney pelves, the fourth case at last is subjectively restored although colibacilluria is present.

Among the four cases with a lasting fistula occurring after the operation concretions have been found in three, the fourth showed a large hydronephrosis.

It is made evident by the above that it generally is not satisfactory to treat the PA PYEL by incision and drainage. In nearly all of the cases there has been some serious disease in the kidney or urinary system, such as concretions pyonephrosis, infected hydronephrosis etc. It is therefore indispensable that the presence of these other diseases be established so that the operative treatment may be directed against these too.

### Conclusions.

1) A survey of 32 cases of operated perirenal abscesses has been made to judge the result of the mode of treatment, which in all cases consisted of incision and drainage, in one case combined with

pyelostomy. Furthermore, the intention has been to investigate if the kidney may have any sequelae of a perirenal abscess.

2) The patients have been divided from an etiological viewpoint into two groups. The author like most others considers every perirenal abscess to be secondary to a renal disease, and with this renal disease as the ground of classification the two groups are mentioned:

I. *Abscessus perirenalis pyonephriticus*.

II. *Abscessus perirenalis pyelonephriticus*.

If the primary renal disease is a pyonephritis, that is a suppurative infection only affecting the parenchyma, the perirenal abscess is placed in the first group. The abscess in the second group has come from a pyelonephritis that is often complicated, *e. g.* with a calculus. Essential to the differential diagnosis between the two abscesses are the patients' history, the laboratory tests of the urine and the X-ray findings.

3) By means of urography a fixation of the kidney (no displacement at all or a movement at the most of  $1/2$  the height of a vertebra upon a change of position of the patient) on the operated side has been established at re-examination in six cases in the first group and in one in the second group. One patient in the first group also revealed a deformation of the kidney pelvis, which was believed to be due to an inflammatory shrinking.

The renal fixation seems to be without any injurious effect to the function of the kidney.

4) Out of the 18 patients who were placed in group I four have died, two in association with the operation, and the other two at a later date from a disease not related to the perirenal abscess.

The cases now living are entirely well or have only slight symptoms from the urinary system.

In group II ten of the fourteen patients have died, four in connection with the operation. Of the six who died later the cause of death in four cases only was not directly associated with the perirenal abscess. Of the four cases still living two have persisting fistulae in the scar 5 and 11 years following the operation. The other two cases are subjectively well, both however have remaining infections of the urinary tract and urography of one of them showed a dilated kidney pelvis.

5) Since the prognosis of the two groups is considerably different a careful urological examination should be made before the



operation upon the abscess, to determine in which group the abscess should be classified. If a pyonephritic perirenal abscess is diagnosed, the operation may be limited to incision and drainage, provided that a kidney carbuncle is not present.

If a pyelonephritic perirenal abscess is diagnosed, the operation must also be directed against the primary disease. In the event that the patient's general condition is severely affected it may be necessary that he is operated upon in stages.

### Summary.

32 cases of perirenal abscesses, who have all been treated with incision and drainage, have been divided into two groups according to their different etiology, a pyonephritic and a pyelonephritic group. The prognosis in the pyonephritic group has been much better than in the pyelonephritic, and the treatment here seems to have been quite sufficient. In the pyelonephritic cases one must direct the operation against the primary renal disease (calculus etc.), if so is not done a fistula can remain after the incision for several years.

At the re-examination many years after the infection the mobility of the kidney has been studied in 13 patients. In six cases of the pyonephritic group and in one of the pyelonephritic the kidney has been found to be fixed.

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## Is Spinal Anaesthesia Always a Reliable Method of Inducing Vaso-Dilatation in the Toes?

By

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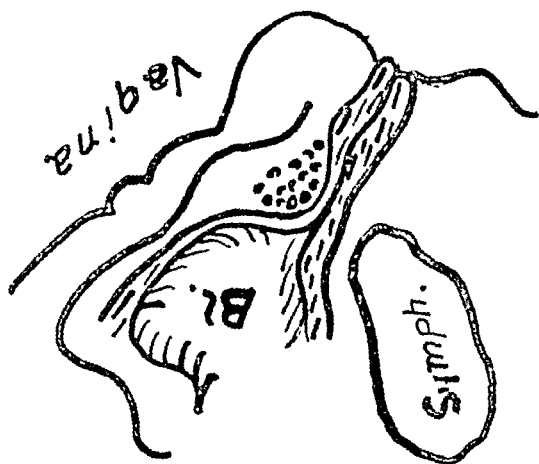
In ascertaining the nature and degree of circulatory disturbance in the legs it is often very useful to induce maximum vaso-dilatation in the legs and simultaneously to measure the skin temperature of the toes.

The various procedures which induce vaso-dilatation by raising the subject's body temperature all suffer from the weakness that the vaso-dilatation occasionally fails to materialise. For this reason, UPRUS, GAYLOR and CARMICHAEL (1) strongly criticise the method devised by LEWIS (2) of raising body temperature by means of a heated chamber. LARSSON (3) does not either obtain satisfactory results with this method. The procedure introduced by GIBBON and LANDIS (4) whereby vaso-dilatation is induced in the toes by holding the hands and forearms in hot water is better but yields unsatisfactory results in 10 % of cases (MONTGOMERY, NAIDE and FREEMAN (5)). A combination of these two methods is said, however, to be fairly satisfactory, though not absolutely reliable (ALLEN, BARKER and HINES (6)). In our Department we have for a long time induced a rapid and considerable rise in body temperature by placing the subject in a bath of hot water with his feet outside, but even this method sometimes fails (LINDQVIST and NÄSLUND (7)).

The methods which are designed to interrupt the sympathetic vaso-constrictors do not either yield consistently satisfactory results. In one's attempt to block a peripheral nerve or the sympathetic chain one may miss the mark. The intravenous injection

formed.<sup>1</sup> The observation period for these cases ranges from 6 months to 4 years.

There is only one drawback to this operation, which was first used for incontinence by NATVIG, *i. e.* it can not be applied in all cases. It is contra-indicated for women in the fertile ages, it can



not be used where the uterus is enlarged and it is difficult to perform technically when the vagina is narrow. In order to achieve an elevation of the neck of the bladder and a support for the fundus with the slightest possible trauma, I have through incision in the anterior fornix grafted bone-chips from the tibia behind the neck of the bladder between the cervix uteri and the wall of the bladder. (See the figure.)

*Technique:* Portio is drawn down by forceps. A small transverse incision is made in the anterior fornix and the posterior wall of the bladder is laid free from the cervix uteri so that a piriform space is shaped behind the neck of the bladder. The drawn portio is covered by a compress and without contamination 5—7 cc bonechips are inserted. The bone tissue can conveniently be taken through a small osteotomy on the medial side of the upper part of the tibia. The material should for the greater part consist of cancellous bone which combines better in healing with the soft parts than the cortical chips. The material can easily be excised with a spoon.

It can be mentioned in this connection that if the transposition of the uterus is used as incontinence-operation the fundus uteri should be well fixed under the symphysis *e. g.* by means of sutures

<sup>1</sup> One of these operations has been performed by Dr G. SUNDSTEN, Gyn. Klin. Eskilstuna Hospital.

*Case 1. A. B. Telegraphist, 35 years. No. 3203/47.*

He has suffered from weakness of his back for 4 years and occasionally from pain in both feet which has been attributed to flatfoot. During the autumn of 1947 he sometimes observed tender blue lines running from the dorsum of his left foot halfway up his leg. They disappeared only to reappear in a slightly different position. For several years he has suffered from occasional pain in the calves on walking long distances. Recently the front of his left foot has felt numb and the toes have been white and cold. At the end of November 1947 the toes of the left foot became very painful, tender and swollen.

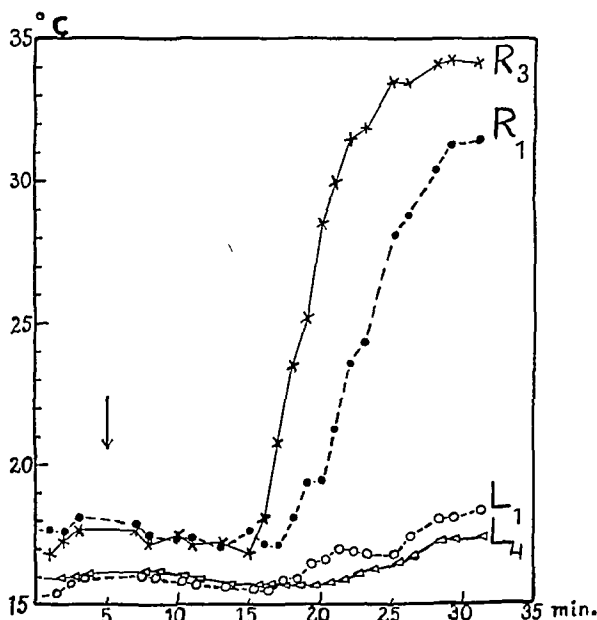


Fig. 1. Skin temperature of the toes of case 1 after immersion of the body into a hot bath at ↓. R<sub>3</sub> temperature of the 3rd right toe etc.

He was admitted on the 3rd December 1947. Routine medical and neurological examination revealed the following abnormalities: the left hallux and part of the second toe were purple in colour; thrombophlebitis of fairly recent origin was present in a superficial vein on the dorsum of the left foot as far as the ankle; a somewhat older thrombophlebitis was present just below the middle of the leg on the medial surface of the left tibia; the pulse in the left posterior tibial and dorsalis pedis arteries could not be felt with any certainty; oscillometry revealed that the circulation in the lower half of the left calf was inferior to that on the right.

A recording of the skin temperature of the toes while the body temperature was raised is shown in Fig. 1. The circulation on the left is very poor, on the right satisfactory.

Fig. 2 shows the skin temperature of the toes while 800 mg. of TEAB was slowly injected intravenously. Once again the circulation is good on the right and poor on the left.

On the 18th December 1947, arteriography was performed on the vessels of the left lower limb. The femoral, anterior tibial and popliteal arteries appeared normal. The main trunk below the formation of the anterior tibial artery was strikingly narrow and only 3 cm. contained contrast medium. At the end of this trunk a medial and lateral collateral could be seen. Neither the anterior tibial nor the peroneal artery were outlined.

This investigation was carried out under spinal anaesthesia and the skin temperature of the toes was recorded at the same time. Before the investigation began, the temperature of the toes was 20–23° C—somewhat higher on the left than on the right side. The anaesthesia was

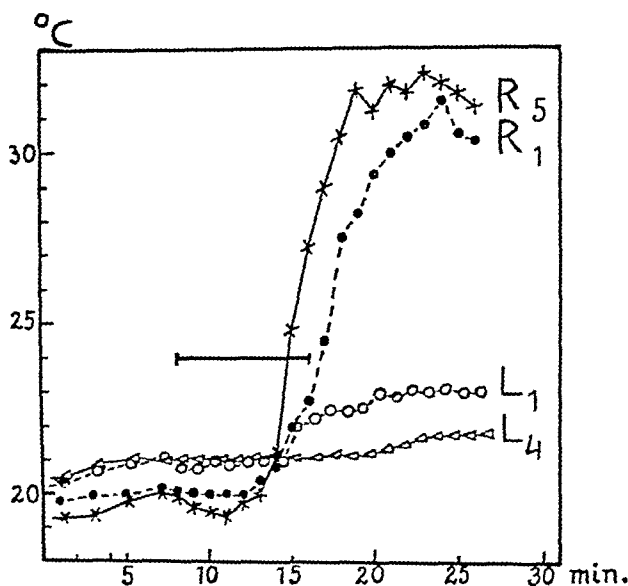


Fig. 2. Skin temperature of the toes of case 1 on injection of 800 mg. of TEAB intravenously. — time of the injection. R<sub>5</sub> temperature of the 5th right toe etc.

completely satisfactory and extended slightly above the symphysis. The skin temperature of the toes was recorded for 40 minutes after the commencement of anaesthesia, during which time it rose 1.1–1.7° on the right and 0.2–1.1° on the left.

The diagnosis must be Buerger's endangitis obliterans in the left leg, both phlebitis and arteritis being present. No pathological changes could be demonstrated with any certainty in the right leg. Skin temperature recordings while the body temperature was raised and after the injection of TEAB show that the circulation in the right foot is good. Nonetheless a perfectly satisfactory spinal anaesthesia scarcely raised the temperature of the toes.

*Case 2. A. S. a former manual worker, 64 years. No. 1139/48.*

In September 1946 an iron beam weighing 100 kg. fell on the patient's right foot. X-ray examination revealed no bony injury. He suffered

fairly severe pain which became worse during the months that followed. Ever since then he has had severe pain in the right foot, frequently extending up the leg. The big toe and the region of the foot immediately proximal to it feel numb. The foot feels very cold and is sensitive to changes in temperature. When the patient walks the foot swells and the pain increases. The patient also suffers a lot from pain in the back.

Examination revealed paresis of the whole right leg with moderate atrophy and increased knee and ankle jerks on the same side. Neurological examination revealed no other abnormality. The C. S. F. was

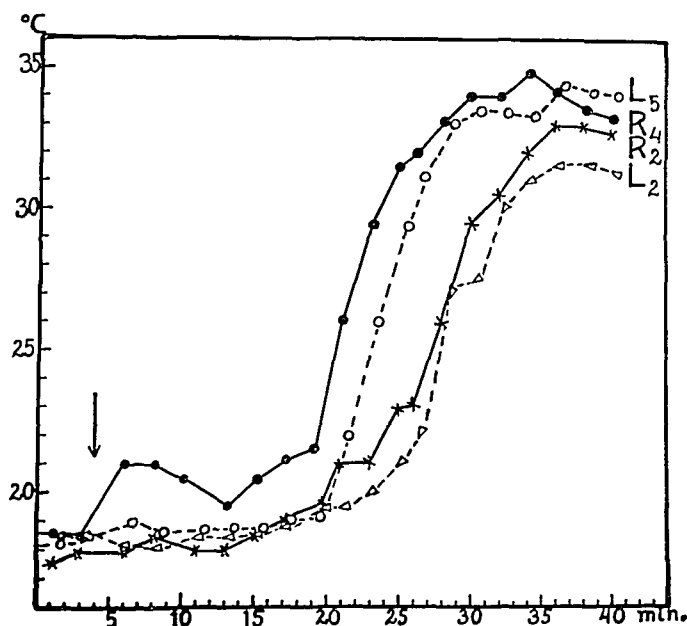


Fig. 3. Skin temperature of the toes of case 2 after immersion of the body into a hot bath at ↓. L<sub>5</sub> temperature of the 5th left toe etc.

normal. The dorsalis pedis arteries could be felt pulsating normally on both sides. Oscillometry yielded satisfactory results on the calves and just above the malleoli, and there was no difference between the two sides. X-ray examination of the right leg revealed extensive calcification in the vessels.

A recording of the skin temperature of the toes while the body temperature was raised by the method described above showed that the increase in temperature of all the toes was very good with the possible exception of the left second toe, the final temperature of which was only 31.5° C. The temperature of the other toes rose to at least 33° (Fig. 3). Thus there is no reduction in the supply of blood to the foot.

Under spinal anaesthesia, on the other hand, the temperature of the toes rose very much less. Although the anaesthesia extended 5 cm. above Poupart's ligament on both sides there was an insignificant rise in temperature. The temperature of the left leg prior to anaesthesia ranged between 20.0 and 21.2°, and at the end of the test it had risen

to 22.5—24.8°. On the right, the temperature rose from 20.0—20.5° to 23.5—26.2°. The rise in temperature was therefore far from complete.

The neurological condition may well be attributed to the trauma (cf. BARRÉ (19)). The pronounced calcification of the vessels of the leg suggests that there may also be a reduction in the supply of blood to the foot and that some of the trouble might arise from this but the good pulsation in the feet and the satisfactory result of oscillometry point the other way. The fact that there was a normal rise in the temperature of the toes when the body temperature was raised shows that the circulation in the toes is satisfactory. The small rise in the skin temperature of the toes during a technically successful spinal anaesthesia would have been interpreted as proof of organic obstruction in the foot's blood supply and led to a faulty diagnosis had not the result of the other test been available. Thus in this case spinal anaesthesia was less effective in dilating the vessels of the feet than was raising the body temperature by means of a hot bath. The positive result obtained from the latter test cannot be due to faulty technique and must be accepted.

It is therefore clear that a faultless spinal anaesthesia does not necessarily induce good vaso-dilatation in the feet even if there is no obstruction of the vessels.

How is one to explain the fact that vaso-dilatation after spinal anaesthesia was particularly inadequate in these cases?

It is possible that there are certain anatomical variations to explain it *i. a.* that in some persons the sympathetic supply to the legs leaves the cord by way of the lower thoracic rather than the upper lumbar segments.

The explanation is probably a very different one, however. There has been some disagreement as to the order in which the various types of nerve fibre are affected by a nerve block. According to MAXTON (20) and EVANS (21) the order is as follows: pain, temperature, touch, proprioception, motor and sympathetic fibres. According to HEIMBECKER, BISHOP and O'LEARY (22) the order is as follows: vaso-constrictors, temperature, pain, motor, joint sense and touch. The most thorough work in this field appears to have been done by SARNOFF and ARROWOOD (23), who reach the following conclusion: "There is no single regular sequence of events but either the sympathetic fibres or the fibres concerned with the appreciation of pinprick may be blocked first." Usually the two types were blocked at about the same time, but the writers



could in some cases by means of differential spinal block arrive at time intervals of as much as 45 minutes between the loss of function in the two types of nerve fibre.

This investigation shows therefore that it should cause no surprise if spinal anaesthesia induces only a partial vaso-dilatation in the toes, or none at all, even when pain sense has been lost all over the leg. This fact has evidently been almost completely ignored hitherto but is extremely important. The true evaluation of the results of vaso-dilatation tests under spinal anaesthesia requires, however, a knowledge of the frequency of such failures as well as of the fact of their occurrence. An investigation on these lines is strongly called for.

### Summary.

Spinal anaesthesia has hitherto been regarded as the most reliable method of inducing vaso-dilatation in the toes. In this paper, a case of Buerger's disease is described in which there was considerable arterial occlusion in the left leg and in which the toes of the right foot underwent a normal rise in temperature when the body temperature was raised or the sympathetic ganglia were blocked with TEAB. Spinal anaesthesia, on the other hand, although it abolished sensation to a point above the symphysis did not cause any vaso-dilatation in the toes. In another case, in which a recording of the skin temperature of the toes while the body was heated showed that there was a good blood supply to the feet, spinal anaesthesia induced a very unsatisfactory vaso-dilatation. Thus spinal anaesthesia is not an absolutely reliable method of inducing vaso-dilatation in the toes and it may yield very misleading results. This appears to have been almost completely ignored hitherto.

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## Treatment of Malleolar Fractures According to Lauge Hansen's Method. Preliminary Results.

By

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In 1942 LAUGE HANSEN defended his doctoral dissertation on Ankle Fractures. Since that time his methods of treatment have stood their test in several Danish hospitals. As so far LAUGE HANSEN's work (1, 2) has been published in Danish only, the author intends to give a brief account of his classification of ankle fractures, his methods of reduction, and the results obtained.

LAUGE HANSEN produced malleolar fractures experimentally, and by roentgen and minutely patho-anatomical examinations he classified these fractures according to their pathologic anatomy into 5 different groups, each with its own characteristic roentgenogram. On the basis of his knowledge of the pathologic anatomy of the fractures he framed methods of conservative reduction of the different types of fracture. By a review of the roentgen examination of 229 cases of malleolar fracture he showed that approximately 99 % of all malleolar fractures met with in clinical work could be grouped according to his principles without difficulty. The methods of reduction were applied to 86 cases of anklefracture, and in practically all cases reduction to anatomically correct position was accomplished.

The conclusions of LAUGE HANSEN's works are briefly as follows:

1. The pathological condition of ankle fractures has been explained in detail as far as 99 % are concerned.
2. A system of classification has been created, which is in con-

formity with the pathologic anatomy and is based on the roentgen examination.

3. Reduction to anatomically correct position can now be carried out conservatively in nearly all cases.

### Nomenclature.

LAUGE HANSEN introduced a new nomenclature, based on the principle that the name of each type of fracture indicates the movements which have produced the fracture. Each type of fracture is divided into various stages, so that the number of the stage indicates the number of lesions of bones and ligaments.

Each designation is composed of two words. The first word is either *supination* or *pronation*, by which the physiological movements are understood (in Anglo-Saxon literature called "inversion" and "eversion"). The second word is *eversion*, *adduction*, *abduction*, or *dorsiflexion*, all indicating the pathological movements between the talus and tibia (*dorsiflexion*, however, only an increase of a physiological movement beyond the normal). By *eversion* is understood an outward rotation of the talus and the foot around a vertical axis (in normal anatomical position), *inversion* is the reverse movement. *Adduction* and *abduction* are movements around a horizontal sagittal axis running at a varying height above the talus, so that these movements are not mere lateral displacements of the talus, but a combination of rotation and lateral displacement of this bone.

### Types of Fracture and Methods of Reduction.

#### *Supination-Eversion Fractures:*

*Mechanism of production:* The supinated foot is everted, *i. e.*, the tip of the foot is turned outward around a vertical axis. Owing to the supination ligamentum deltoideum is relaxed, and the first thing that happens is

a lesion of ligamentum malleoli lateralis anterioris (it may be accompanied by avulsion of a bone shell at one of the attachments) (stage I).

Now the lateral malleolus may rotate a little outward, but ligamentum interosseum and ligamentum malleoli lateralis posterioris are intact. Continued outward rotation will therefore produce an oblique spiral fracture involving the lateral malleolus and the distal part of the fibula (stage II).

By continued movement the pull exerted by ligamentum malleoli lateralis posterius will produce

*an avulsion fracture of the posterior lip of the tibia* (or the ligament ruptures) (*stage III*).

At that time ligamentum deltoideum is tightened and causes, if the movement is continued,

*a fracture of the medial malleolus* (or the ligament ruptures) (*stage IV*).

Further outward rotation of the foot may in some cases give rise to *a torsion fracture of the tibia* (*stage V*) and of the fibula (*stage VI*).

As appears from this some of the injuries may be either a fracture or a ligamentous lesion. However, within each type of fracture one lesion will always be present as a fracture if the stage in question has been reached. This fracture, which is generally situated in the fibula, may thus be used in the determination of the type.

*The characteristic feature of the supination-eversion fracture is the oblique spiral fracture involving the lateral malleolus and the adjacent part of the fibula.*

*Reduction:* The underlying principle of the reduction manoeuvres is that movements of the foot in the opposite direction and in the reverse sequence should be carried out.

Stages II, III, and IV: The anesthetized patient is placed in dorsal position with knee and hip of the fractured extremity flexed at right angles. The extremity is fixed by an assistant holding just proximal to the knee, and the operator grasps the heel with one hand, and the fore and mid foot with the other, and the reduction is carried out as follows:

1. The movements producing the fracture are first performed, *i. e.*, the supinated foot is turned outward, and then plantarflexed. These movements "unlock" the fracture if it has been impacted.

2. By a very vigorous pull at the heel of the plantarflexed foot the proximal displacement of the fragments of the posterior lip of the tibia and lateral malleolus is corrected. The pull must be exercised in the longitudinal direction of the crus.

3. By pressure on the posterior surface of the heel the foot is brought forward while another assistant presses backward on the distal part of the crus. By this procedure the backward displacement of the two said fragments and of the talus is overcome.

4. The foot is inverted maximally, *i. e.*, the tip of the foot is turned medially around an axis running in the longitudinal direc-

tion of the crus, by which the outward rotation of the lateral malleolus and the diastasis between the latter and tibia are overcome; and then the foot is pronated.

5. The plantarflexed foot is moved upward until it forms a right angle with the crus.

6. The plaster cast is then applied while an assistant holds the foot in the position described, which may be done without difficulty if only the foot is kept carefully pronated all the time by a grasp around the metatarsal bones.

7. Facing the fractured foot the operator places the bandaged extremity between his heteronymous arm and thorax. While the plaster is hardening, he exerts a medial pressure on the heel region with the homonymous hand, and a counterpressure on the medial malleolus with the palm of the other hand. In this way any remaining lateral dislocation of the talus and medial malleolus will be corrected. At the same time the assistant pronates and inverts the anterior part of the foot so vigorously that it comes into maximal pronation, and that the longitudinal axis through the crus runs through third or fourth toe.

In stage I (and stage II without backward or proximal displacement of the lateral malleolus) the procedures numbered 4, 5, 6, and 7 will suffice. In stages V and VI the tibial fracture is treated according to the usual principles, the malleolar fracture as described above.

#### *Supination-Adduction Fractures.*

*Mechanism of production:* The maximally supinated foot is supinated and adducted in the talocrural joint, thereby causing an avulsion fracture of the lateral malleolus (or lesion of ligamentum calcaneofibulare) (stage I).

Owing to the pressure exerted by the talus on the medial malleolus the next lesion will be

a fracture of the medial malleolus (stage II).

*The characteristic feature of this type of fracture is the transverse fracture of the lateral malleolus on a level with or distal to the articular surface of the ankle joint.*

*Reduction:* Stage I: After application of the plaster cast the heel region is abducted, and the fore part of the foot is pronated and everted a little while the plaster is hardening. Stage II: The foot is moved laterally and frontally; then the same procedures as in stage I.

*Pronation-Eversion Fractures.*

*Mechanism of production:* When the foot is pronated, ligamentum deltoideum is tightened. If the foot is then everted, i. e., turned outward around a vertical axis, the result will be

*a fracture of the medial malleolus* (or lesion of ligamentum deltoideum) (*stage I*).

Owing to the laxity caused hereby there will, in addition to the eversion movement, also come a certain lateral effect of the pressure and *ligamentum malleoli lateralis anterioris and ligamentum interosseum will rupture* (or shells of bone may be torn off at the sites of the ligamentous attachments) (*stage II*).

Now the fibula may rotate outward, more particularly the distal part, and at a varying height above the ankle joint

*a torsion fracture of the fibula* is produced (it may be situated in the neck) (*stage III*).

The pull at ligamentum malleoli lateralis posterioris will then give rise to

*a fracture of the posterior lip of the tibia* (or the ligament may rupture) (*stage IV*).

Further outward rotation may in some cases cause

*a torsion fracture of the tibia* (*stage V*).

*The characteristic feature of this type of fracture is the high fracture of the fibula.*

*Reduction:* As in supination-eversion fractures, yet so that the foot is pronated and everted at the same time.

*Pronation-Abduction Fractures.*

*Mechanism of production:* When the foot is maximally pronated, ligamentum deltoideum is tightened. If an additional pronation between the tibia and talus occurs, and/or the talus is displaced laterally,

*a fracture of the medial malleolus is produced* (or ligamentum deltoideum ruptures) (*stage I*).

Then the lateral pressure will exert its effect on the lateral malleolus and

*ligamentum malleoli lateralis anterioris et posterioris will rupture* (or a shell of bone may be torn off at one of the sites of attachment) (*stage II*).

After this the foot and the lateral malleolus may be carried further in lateral direction, causing

*a bending fracture of the fibula a little above the ankle joint (stage III).*

*The characteristic feature of this type of fracture is the bending fracture of the fibula a little above the ankle joint.*

*Reduction:* Stages I and II: After application of the plaster cast the heel region is adducted and the fore part of the foot is pronated and inverted while the plaster is hardening. Stage III: The foot is moved frontally and medially, and then the same procedures as in stages I and II.

#### *Pronation-Dorsiflexion Fractures.*

*Mechanism of production:* By forced dorsiflexion of the pronated foot the pressure exerted by the talus on the tibia and medial malleolus will in the first place produce

*a fracture in the basis of the medial malleolus (stage I),*  
and in the second place

*avulsion of a large fragment at the anterior lip of the tibia (stage II).*

Owing to the laxity thereby caused the talus may now be moved forward and the pull at the ligaments gives rise to

*a fracture of the fibula at a distance above the ankle joint (stage III).*

Finally, the pull of the ligaments at the posterior aspect of the ankle joint may cause

*a fracture of the posterior lip of the tibia (stage IV).*

*The characteristic feature of this type of fracture is the large fracture of the anterior lip of the tibia.*

*Reduction:* LAUGE HANSEN states that it is doubtful whether closed reduction is feasible. In the case presented in this paper the result was medium. The reduction was accomplished by a vigorous pull distally under simultaneous plantar flexion of the foot and pressure against the fragment of the anterior lip of the tibia. Our experience with this type of fracture is, however, not sufficient to recommend a general method of reduction.

#### *Other Fractures.*

† Among approximately 200 fractures LAUGE HANSEN found only 2, the roentgenogram of which did not correspond to any of the types of fracture described above. Both these fractures had been produced by direct violence. In the material presented here there were 3 cases out of 203, which could not be classified according to LAUGE HANSEN's principles. All three cases were longitudinal



fractures of the lateral malleolus, resulting from direct trauma to this bone.

According to various authors 2—3 % of all malleolar fractures are *isolated fracture of the posterior lip of the tibia*. This type of fracture did not occur among LAUGE HANSEN's approximately 300 cases. In the total material of the author comprising approximately 400 cases, this type of fracture has not been diagnosed either. As the fibular fracture in the pronation-eversion type may be found in the neck of the fibula, the diagnosis "isolated fracture of the posterior lip of the tibia" cannot be made unless the entire crus has been examined roentgenologically with negative result. It does not appear from the various publications on "isolated fracture of the posterior lip of the tibia" whether the roentgen examination has comprised the entire crus; hence one must so far be sceptical with regard to the occurrence of this type of fracture.

An example of the importance of the roentgen examination of the entire crus and of the presence of the ligamentous lesions is seen in the illustrations.

After a trauma to the ankle joint a patient was referred to roentgen examination, which showed a small avulsion from the posterior lip of the tibia, and the ankle joint gaped perhaps a trifle at the medial malleolus (Fig. 1 and 2). In most cases this would presumably be diagnosed as a sprain of the ankle. If, however, the examination is extended to comprise the entire crus, a fracture about the middle of the fibula is found, and accordingly it may be diagnosed as pronation-eversion fracture, stage IV. This diagnosis is verified by a roentgenogram of the ankle taken while the foot is turned outward by the hand. Lateral subluxation of the talus and pronounced diastasis between the tibia and fibula is found (Fig. 3). In the case described here the first and second lesions were thus exclusively represented by ligamentous injury.

### Follow-up Examination.

#### *Material.*

The material reported here comprises all the cases of ankle fracture treated in the Surgical Department from November 1, 1942, to November 1, 1946. A total of 203 cases has been treated. Three of these cases have not been included in the report because they were not admitted to hospital until 3—4 weeks after the occurrence of the fracture, and so it might be anticipated that reduction of these fractures would prove impossible.

The follow-up examination took place at least 12 months after

the accident. Out of 200 cases 116 were men, 84 women, a distribution roughly corresponding to that found in other reports. Cases of epiphyseal separation have not been included.

Table 1 shows the distribution among the various types of fracture:

Table 1.

	Randers	Lauge Hansen's doctoral dissertation	Karolinska Sjukhuset (1940—42)
Supination-eversion fractures . . . .	85 = approx. 42 %	68.5 %	66.5 %
Supination-adduction fractures . .	29 = " 14 %	15.5 %	9.5 %
Pronation-eversion fractures . . . .	47 = " 23 %	8.3 %	7 %
Pronation-abduction fractures . . .	35 = " 17 %	6 %	12.5 %
Pronation-dorsiflexion fractures . .	1		
Fractures from direct violence . . .	3		

The degree of severity as it is expressed in the distribution among the various stages of fracture appears from Table 2.

Table 2.

Stage	I	II	III	IV	V	Direct fractures	Total
Total number . . . . .	24	71	45	49	8	3	200
Number followed up . . . . .	16	52	30	44	5	2	149
Percentage followed up . . . . .	66	73	66	90	62	66	74
Details <sup>1</sup> received from Accident Insurance Board . . . . .	2	4	2	1	0	0	9

If the material is divided into two groups, namely the comparatively mild fractures (stages I and II) and the comparatively severe fractures (stages III, IV, and V), it is seen that the proportion between mild and severe cases is essentially the same primarily and at the follow-up examination.

### *Reduction and Immobilization.*

In 120 of our 200 patients it was necessary to reduce the fractures. 115 were reduced once; in 106 cases the result was good, in 8 medium, and in 1 case the result was poor, which was, how-

<sup>1</sup> Only one of these patients has been subjected to roentgen examination.

ever, not found out until a subsequent revision of the roentgenograms. 4 cases were reduced twice; 1 with good result, 2 medium and 1 poor (also in this case the roentgenogram had been misinterpreted). In spite of 3 attempts at reduction the result was poor in 1 patient, and no further attempts were made.

*Open reduction, osteosynthesis, and wire extension have not been employed.*

Only on a single point the treatment has deviated from LAUGE HANSEN's technique, *i. e.*, with regard to the time of reduction. According to LAUGE HANSEN the reduction should preferably be carried out immediately on the occurrence of the fracture. However, a large number of our patients was not admitted to hospital until one or two days after the accident, and had then a considerable swelling. Accordingly we often postponed the reduction for a couple of days until the swelling had subsided considerably, and we have not experienced any difficulties which might be ascribed to the postponement. The reduction was always carried out under ether anesthesia, except in stages I and II with only inessential displacement. After the reduction a tight-fitting plaster cast was applied, extending from the knee to the proximal phalanges of the toes, and incorporating a posterior splint reaching a little beyond the toes. The use of a completely unpadded plaster cast has only in a few cases caused inconsiderable pressure sores, and we have never observed any paralysis owing to the pressure of the cast.

If the control roentgenograms showed good position, a rubber-covered wooden block, serving as a heel, was incorporated two or three days later, and normally the patients were allowed to get out of bed and were discharged after another couple of days. The time in bed after the application of the plaster cast averaged 4.2 days for such cases as were not complicated with other affections.

As, undoubtedly, the tendency to secondary displacement increases with the number of lesions, *the time in which the retention dressing has been applied* has been regulated, not only by the age of the patient, but also by the stage of the fracture. In some of our patients the dressing has undoubtedly been removed too early, and we now advise the following periods of dressing: Stage I 4—5 weeks, stage II 5—6 weeks, stage III 7—8 weeks, and stages IV, V, and VI 9—10 weeks.



Fig. 3.



Fig. 2.



Fig. 1.



## Classification and Results.

The radiological results of the reduction have been characterized as *good*, *medium*, or *poor* on the following lines:

In order to classify the result as *good* the author has required the following:

The *talus* shall be reduced to anatomically correct position; special care should be taken to bring it sufficiently forward.

There must be no lateral displacement of the *lateral malleolus*, and its posterior displacement must not exceed 2 mm.

In the supination-eversion fractures the fracture line in the fibula often gapes a little upwards, which is due to the fact that the fragment has not been pulled sufficiently in distal direction before the foot is pushed forward. Diastasis in the proximal part of the fracture line is, however, of no importance if only the malleolus itself has been pushed sufficiently forward, which is the case when the anterior contour of the fibula is unbroken.

If more than a thin shell of bone has been torn off from the *posterior lip of the tibia*, the fragment must not be displaced more than 2 mm.

There must be no lateral displacement or angulation corresponding to the *medial malleolus*, and the fracture line in the latter must not gape more than 2 mm.

It may sometimes be difficult to secure contact between the broken surfaces of the medial malleolus, but in some cases the author has successfully overcome this difficulty by placing a narrow roll of paper bandage under the plaster just distal to the medial malleolus. This roll should then be pressed proximally and laterally by an assistant while the plaster hardens. If the plaster cast has already been applied, the malleolus may be pressed into its normal place in the same way through a small window in the plaster.

As far as the *tibial fractures* (stage V) are concerned, the author has required that there must be no angulation, and that the lateral displacement must not exceed a few millimetres.

The result has been described as *medium* in cases where the lateral malleolus has been displaced 2—5 mm backward and/or up to 2 mm laterally, and/or if the fragment of the posterior lip of the tibia has been dislocated 2—5 mm, and/or the fracture line in the medial malleolus gapes 2—5 mm without angulation. On the other hand, the talus must be reduced to anatomically correct position. Tibial fractures must at most be angled 10°.

The result has been characterized as *poor* in cases with displace-

ment of the talus or angulation between this bone and the tibia, and in cases with lateral displacement of the medial malleolus or angulation corresponding to it. The same applies to cases where the lateral malleolus has been displaced more than 5 mm backward or more than 2 mm laterally, or if the fragment of the posterior lip of the tibia is dislocated more than 5 mm, or if the diastasis in the medial malleolus amounts to more than 5 mm. Cases with an angulation exceeding  $10^{\circ}$  in the tibial fractures, or larger lateral displacement, or shortening have also been classed as poor.

*The condition at the follow-up examination* has been evaluated with a view to the *subjective, clinical, and radiological results* on the following lines:

*Subjective result: Good:* No discomfort during the daily movement of the patient, and only slight discomfort by extra strain.

*Medium:* Daily discomfort, but usual work carried out to the same extent and at the same remuneration as before the accident, or severe discomfort by extra strain.

*Poor:* Reduced capacity for work.

*Clinical result: Good:* Natural position of the foot; natural gait; painfree movements; and all movements of the ankle joint and foot at least one half of the value of the unaffected side.

*Medium:* Natural position of the foot and natural gait, but at least one of the movements of the ankle joint or foot reduced to less than one half of the value of the unaffected side.

*Poor:* Deformity, inter alia, unilateral flatfoot, or disturbances of gait.

*Radiological result:* As described under the radiological result of reduction. Cases with good position, but slight arthrosis have been classified as medium, cases with severe arthrosis as poor. If pseudoarthrosis was present, the case was classified as poor unless it was a question of non-union of a small avulsion.

The three methods of classification are not absolutely congruent, but yet roughly so. The subjective result gives an impression of the social importance of these lesions. On the other hand, the clinical and radiological results indicate to which extent we have succeeded in achieving normal anatomical and physiological conditions. The radiological classification used is very strict, but gives only little scope for discretion in the evaluation.

### *Supination-Eversion Fractures.*

A total of 45 men and 40 women was treated, and 31 men and 29 women have been followed up. Moreover, from the Accident Insurance Board details of 1 man and 1 woman have been received.

Table 3.

	Subjective result						Clinical result						Radiological result					
	I	II	III	IV	V	to- tal	I	II	III	IV	V	to- tal	I	II	III	VI	V	to- tal
Good .....	1 (+1)	14 (+1)	8 (+1)	25	1 (+2)	49	1 (+1)	16 (+1)	8	24	1 (+1)	50	1	16	8	19	1	45
Medium .....	0	3	0	5	1	9	0	1	0	3	0	4	0	1	0	5	1	7
Poor .....	0	0	0	2	0	2	0	0	0	5	1	6	0	0	0	8	0	8

Figures given in parenthesis represent patients of whom details have only been received through Accident Insurance Board.

The causes of the poor results were:

Poor subjective result: 2 patients.

1 patient had a complicated fracture resulting in pyarthrosis, which was healed by penicillin treatment without incision. There is now total ankylosis of the ankle joint.

1 patient showed loss of dorsiflexion with a slightly limping gait without pain at the follow-up examination. She considered herself unable to resume her work as a charwoman. By roentgen examination nothing abnormal could be demonstrated (compensation neurosis?).

Poor clinical result: 7 patients.

1 patient had total ankylosis of the ankle joint owing to pyarthrosis.

1 patient showed loss of dorsiflexion.

2 patients showed loss of dorsiflexion and almost loss of pronation and supination.

3 patients showed loss of pronation and supination, whereas the plantarflexion and dorsiflexion were more than one half of the values of the unaffected side. Two of them walked a little more on the outer edge of the foot than is normal.

Poor radiological result: 8 patients.

2 patients had pseudarthrosis in the medial malleolus, but no other radiological or clinical symptoms.

1 patient had pseudarthrosis in the medial malleolus, and the lateral malleolus was dislocated 5 mm backward (secondary displacement). No clinical symptoms.

2 patients had pseudoarthrosis in the medial malleolus with slight radiological arthrosis.

2 patients had severe radiological arthrosis in the ankle joint, but completely normal movability.

1 patient had severe arthrosis and ankylosis owing to pyarthrosis.

#### *Supination-Adduction Fractures.*

In this group a total of 20 men and 9 women was treated, and 13 men and 8 women have been followed up. All showed



good subjective and radiological results; clinically one was medium, the others good. From the Accident Insurance Board details of another three patients have been received. Two of them were subjectively and clinically good, but had not been subjected to roentgen examination. The result of the third case could not be evaluated as a few months after the ankle fracture he had another fracture involving the cuboid and calcaneus.

### *Pronation-Eversion Fractures.*

In this group a total of 27 men and 20 women was treated, and 22 men and 15 women have been followed up. From the Accident Insurance Board details of another 2 men have been received.

Table 4.

	Subjective result					Clinical result					Radiological result				
	II	III	IV	V	total	II	III	IV	V	total	II	III	IV	V	total
Good .....	14 (+2)	6	10	3	33 (+2)	14 (+2)	6	9	3	32 (+2)	14	6	8	2	30
Medium ..	2	0	1	0	3	0	0	1	0	1	2	0	0	1	3
Poor .....	0	0	1	0	1	2	0	2	0	4	0	0	4	0	4

Figures given in parenthesis represent patients of whom details have only been received through Accident Insurance Board.

The causes of the poor results were:

Poor subjective result: 1 patient.

Constant discomfort owing to stiffness of the ankle joint; was primarily poor in spite of three attempts at reduction. The clinical and radiological result was also poor.

Poor clinical result: 4 patients.

1 patient had almost total ankylosis in the ankle joint with a pronounced limp (it was the patient with poor subjective result).

2 patients showed almost total loss of pronation and supination, one of them also loss of dorsiflexion, but had otherwise normal movability.

Both slightly dragged the leg in question.

1 patient walked with a slight outward rotation of the foot; the movements were completely normal; by roentgen examination nothing abnormal could be found.

Poor radiological result: 4 patients.

1 patient had a pronounced backward displacement of the talus and the fragment of the posterior lip of the tibia (was primarily poor).

1 patient had a slight valgus position of the talus (secondary displacement — the splintage had been removed too early). Clinically the result was also poor.

1 patient had a lateral displacement of the talus and the lateral malleolus of 2—3 mm (secondary displacement); no clinical symptoms.

1 patient had a severe arthrosis; the position ideal; clinically poor. Pseudarthrosis was not found in this group.

### *Pronation-Abduction Fractures.*

In this group 21 men and 14 women were treated; 18 men and 11 women have been followed up. Details of one man have been received from the Accident Insurance Board.

Table 5.

	Subjective result				Clinical result				Radiological result			
	I	II	III	total	I	II	III	total	I	II	III	total
Good .....	3	6	14	23	3	6	9 (+1)	18 (+1)	3	8	11	22
Medium .....	0	4	2	6	0	0	4	4	0	0	1	1
Poor .....	0	0	(+1) 0	(+1) 0	0	4	3	7	0	2	4	6

Figures in parenthesis represents a patient of whom details have only been received through Accident Insurance Board.

The causes of the poor results were:

Poor subjective result: None.

Poor clinical result: 7 patients.

3 patients showed loss of or greatly reduced pronation and supination. Before the fracture one of these patients suffered from arthrosis in the talo-calcaneal joint. In one case there was secondary displacement of the talus because the cast had become too wide. A couple of months after the removal of the cast another patient contracted a phlebitis in the limb in question. In this patient there was clinically slight valgus position of the heel, but no flatfoot; by the roentgen examination nothing abnormal could be demonstrated.

2 patients showed loss of or greatly reduced dorsiflexion. In one of them nothing abnormal could be demonstrated by the roentgen examination, in the other a non-united avulsion at the medial malleolus was found.

1 patient showed loss of dorsiflexion and greatly reduced pronation and supination, and walked a little on the outer edge of the foot. By the roentgen examination secondary displacement was found.

In 1 patient approximately 10° valgus position of the talus could be produced passively; the gait was a little stiff, and he stated that if he walked for a long time in loose soil, he had slight pain. By the roentgen examination nothing abnormal could be demonstrated.

Poor radiological result: 6 patients.

2 patients had pseudarthrosis in the medial malleolus, one without clinical symptoms; in the other it was a non-united avulsion, but there was reduced dorsiflexion.

2 patients had lateral displacement of the talus; the roentgenograms taken after the reduction had been misinterpreted. One had no clinical symptoms, the other showed loss of pronation and supination.

1 patient had backward displacement of the talus because the cast had become too wide.

1 patient had severe arthrosis, but the position was good. The mobility was reduced.

### *Pronation-Dorsiflexion Fractures.*

In this group one man was treated (stage IV). The result of the reduction was characterized as medium. Five weeks after the occurrence of the fracture the "walking" plaster cast broke resulting in secondary displacement, which proved impossible to reduce. Subjectively the result was medium; clinically and radiologically poor.

### *Importance of Reduction.*

The material presented here has not been compared with other reports. The reason is that before the publication of LAUGE HANSEN's classification no safe basis of comparison existed. WIDÉN (4) has certainly studied a series of cases from Karolinska Sjukhuset, classified according to LAUGE HANSEN's principles, but he did not say on which lines the results had been evaluated, and accordingly it cannot be used for comparison.

However, of the cases followed up 107 out of 118 cases with displacement (2 misintrepreted cases excluded) were reduced to anatomically correct position. This is supposedly far better than what can be obtained by other methods of reduction. The importance of correct reduction can be seen by a comparison of the end-results of good reductions with those of medium and poor reductions. Their number is, however, too small for sure statistical conclusions.

Of the three poor results of the reduction only one showed good subjective and clinical results, while in one it was subjectively medium and clinically poor, and in one the subjective and clinical results were poor.

In the 10 cases where the result of the reduction was medium (all the patients were followed up), no were subjectively poor. Two of the 10 patients are left out of the evaluation here because

secondary displacement occurred (the cast became too wide or broke). In the remaining 8 the subjective results was medium in three cases, good in five, and in four cases (including the 3 subjectively medium) the clinical and/or radiological results were poor.

Among 137 patients subjected to follow-up examination, in whom the position was good after the reduction, there were 20 with poor results in one or more classes of the follow-up examination. One of these patients is excluded because the fracture was complicated and pyarthrosis occurred, so that 19 out of 136 patients with primarily good result were classified as "poor result" in at least one class of the follow-up examination. Out of these 9 had a poor result only radiologically. As a diversity of opinion exists as to the rôle played by the comparatively small displacements which have made the author classify some of the cases as radiologically poor (their importance, if any, cannot be ascertained until 5 years after the accident), the proportion has been made up between the results of the reduction and the subjective and clinical results found at the follow-up examination. It then appears that of 13 patients with poor or medium result of the reduction 7 had a poor subjective and/or clinical result (however, two of them owing to secondary displacement), while poor subjective and/or clinical results were found only in 10 of 136 patients, in whom the reduction had been classified as good (one of them owing to secondary displacement).

*Pseudarthrosis in the medial malleolus* may be due to defective reduction, interposition of soft parts, or defective fixation. Pseudoarthrosis has been observed in 11 cases of 63 fractures involving this bone. In 4 cases it was a question of small non-united avulsions, 3 of the remaining 7 were symptom-free. The consequent use of "walking" plaster casts has scarcely increased the number of pseudarthroses in the medial malleolus. In a report from Odense where the "walking" plaster cast is not employed, E. HUSFELDT (3) mentions 6 cases of pseudoarthrosis in 47 fractures of the medial malleolus. The difference is not statistically sure, so there hardly seems to be any reason to discontinue the use of this type of cast.

On the other hand, the "walking" plaster cast must be held responsible for the case of secondary displacement that occurred because the cast broke, and possibly also for the case in which the cast became too wide. The remaining three cases of secondary displacement must presumably be ascribed to too short time of

immobilization since these 3 patients were immobilized for periods much shorter than that recommended by the Department.

*The difference in the prognosis* for the various types of fracture can only be vaguely indicated because the material becomes comparatively small by being divided into groups. If again the radiological result is not taken into account, it is seen that *poor subjective and/or clinical results* are found in

supination-adduction fractures in 0 of 23 patients,

supination-eversion fractures in 6 of 61 patients (1 owing to pyarthrosis),

pronation-eversion fractures in 4 of 39 patients (1 primarily poor; 1 owing to secondary displacement),

pronation-abduction fractures in 7 of 30 patients (1 primarily poor; 1 owing to secondary displacement).

Thus in the material reported here there are at least twice as many patients in the group pronation-abduction fractures who have obtained a dis-satisfactory result as in the other groups.

The 10 cases of good reduction, but poor subjective and/or clinical results are distributed as follows: 2 supination-eversion fractures (stage IV), 2 pronation-eversion fractures (stage II) + 1 with secondary displacement (stage IV), 5 pronation-abduction fractures (4 stage II, 1 stage III). This also suggests that the prognosis for the pronation-abduction fractures is poorer than that for the other types of fracture. It must be assumed that — apart from the difficulties of reduction — the prognosis for the pronation-dorsiflexion fractures is poorer than for the other types of fracture owing to the extensive fractures of the articular surface of the tibia, which probably entails a greater possibility of subsequent arthrosis.

### Conclusive Remarks.

A final evaluation of LAUGE HANSEN's methods of treatment can only be made on the basis of a more detailed report of a more extensive material with a longer time of observation. However, there are several reasons for calling attention to his works. The first is the results of reduction: 90 % ideally reduced, and the majority of the remaining 10 % has only comparatively small displacements. Secondly, LAUGE HANSEN's methods render possible a systematic treatment of ankle fractures, so that it now

gives rise to few problems in the daily work of the hospital. Finally, his system has to a great extent reduced the osteosynthesis and wire extension treatment of these fractures, so that the medical work is diminished, and the time spent in hospital is shortened to equal satisfaction for both patients and hospital staff.

### Summary.

On the basis of 200 cases of ankle fracture treated according to LAUGE HANSEN's method the system of classification, manners of production, and mechanisms of reduction are reviewed.

The results of the follow-up examination of 158 of the cases are made up, and strict principles for the classification of the results of the follow-up examination are given.

The pronation-abduction fractures have given the greatest percentage of poor results, whereas no poor results were found among the supination-abduction fractures subjected to follow-up examination.

The importance of the reduction for the end result is emphasized, and an example of the importance of the ligamentous lesions for the genesis of the ankle fracture is given.

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## Benign Tumours of the Stomach. — A Case of Lipoma Submucosa Ventriculi simulating Cancer of the Stomach.

By

HENNING PAABY.

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As benign tumours of the stomach — and in particular lipomas — are of rare occurrence, the publication of the following case may be of interest.

Case record: M. aged 47 years, admitted on Dec. 11th, 1947 (case record No. 1389/47) under the diagnosis: cancer of the stomach — anaemia gravis. Apart from the present disorder, the patient has largely been in good health previously. A brother of his has a gastric ulcer. Otherwise no familial predisposition to disorders of the stomach. Has never had lipoid nodes elsewhere. Six months before admission the patient had melaena and felt very tired. At a subsequent examination there was no blood in the stools. At that time he had no other symptoms from the stomach. Was treated with regulation of the diet for one month. Became free from symptoms until, two months before admission, he developed a tendency to small regurgitations, often the colour of chocolate or coffee grounds. At the same time he had some oppression across the epigastrium, but no actual pain, most frequently coming on immediately after the meals but subsiding in the course of a couple of hours. No large vomitings, nausea, relief of oppression by taking a meal or periodicity of symptoms. No eructation or pyrosis. During the last three weeks before admission the patient felt a highly progressive fatigue, had slight, functional dyspnoea and some headache. The stools, however, were not black. His food agreed with him. His weight decreased a little. In addition he was troubled by some constipation. No symptoms from the urinary tract.

*Objective examination:* Distinctly anaemic. No jaundice or cyanosis. State of nutrition slightly over the average. Not distressed. General

health on the whole not exhausted. The objective examination did not reveal anything abnormal apart from a large intumescence to the right in the epigastrium; it was especially conspicuous in deep inspiration.

*Examinations:* Hgb. 45 per cent., erythrocytes 2.57 mill., col. index 0.91, halometry  $7.1\ \mu$ , thrombocytes 424,840, leukocytes 6,270, differential count nothing abnormal. Red and white blood picture showed nothing abnormal.

Ewalds test meal: M + R: 175 + 38 cc.; congo-phenolphthalein: 20/53, well-chymified, no mucus. Kemp's test meal: 6 hours: large quantity retained. Feces: +, +++ benzidine. Urine: no albumen, sugar or pus. Blood-pressure: 95/70.

*X-ray of stomach:* large defective filling in the pars pylorica, where the contrast medium is seen as a narrow stripe. The border between the corpus and the defective filling is irregular, uneven and ill-defined.

As both the clinical and radiological signs seemed to indicate that this was a case of a large, profusely bleeding cancer of the stomach with severe anaemia, a median superior laparotomy with resection of the stomach *ad modum* Polya was made on Dec. 15th, 1947, under nitrogen monoxide-ether anaesthesia and after preceding blood transfusion.

At operation a smooth, well-defined tumour the size of a fist was found in the pyloric part, developed into the lumen, without infiltration of the wall.

No glandular or hepatic metastases.



Resection preparation. Cut open along the greater curvature. The pylorus to the left. The tumour is seen to project on posterior wall. Lipoma tissue at the bottom of the ulceration (at the centre of the picture).

In the posterior wall of the corpus and the canalis of the excised portion of the stomach, a lipomatoid, soft tumour, measuring  $11 \times 6 \times 4.5$  cm., was found, covered with mucous membrane. It was macroscopically well-defined. Above the centre of the tumour, the mucous membrane displayed an ulceration, measuring  $3 \times 1$  cm., with undermined edges. Tumour tissue was seen at the bottom. The mucous membrane was seen to pass evenly into the tumour tissue without any infiltration at the edges.

*Histological examination:* the tumour is composed of simple fatty tissue with fine, vascularized septa, originating from the submucosa; well-defined. Both at the edge and at the bottom of the ulceration a thin layer of granulation tissue is seen, passing on evenly to the lipoma tissue. At the edge of the ulcer, development of connective tissue, extending partly into the lipoma tissue, partly into the submucosa. No polymorphism anywhere, nor any change of type of connective tissue cells; no signs of malignancy. Otherwise, the mucous membrane is natural, apart from a vigorous lymphocyte- and plasma cell-infiltration near the ulceration. A mesenteric gland displayed nothing abnormal.

*Histological diagnosis:* submucous lipoma. Ulceration of simple type (signed: TAGE LUND).

Bronchopneumonia supervened as postoperative complication, but subsided under treatment with penicillin. Discharged on Febr. 7th, 1948, in well-being. Reply to enquiry 3 months after discharge: complete well-being without any dyspeptic symptoms whatever.

The frequency of benign tumours of the stomach is stated very differently by the various authors. In a material of operations comprising 2,195 cases of tumour of the stomach, 1.3 per cent. was found to be benign (13). Other publications (15, 16, 20, 24, 26) state somewhat higher figures.

It is pointed out in a publication by RIEGLER & ERIKSEN (35) that the actual occurrence is more frequent than supposed, as numerous cases follow a course without any symptoms and are accidentally found on post-mortem examination. In 239 patients with tumour of the stomach who were X-rayed, these authors found 8.8 per cent. with benign tumours. In 6,242 post-mortem examinations, gastro-duodenal tumours were found in 194 cases, 25 per cent. being benign. In a number of 11,000 post-mortem examinations STEWART quote (35) found 263 malignant tumours of the stomach and 47 which were benign (15 per cent.).

As numerous symptomless cases are not submitted to post-mortem examination and as many small benign tumours, in particular leiomyomas, are easily overlooked at this examination, it is undoubtedly correct that the real occurrence of these tumours is more frequent than generally supposed.

The *classification* of these tumours is rather varying. They are divided, according to their histological structure, by MINNES & GESCHICKTER (26) into the following three main groups:

(I) Epithelial, comprising adenomas, adenopapillomas, fibroadenomas and others.

(II) Mesenchymal, comprising leiomyomas, fibromas, lipomas, angiomas and others.

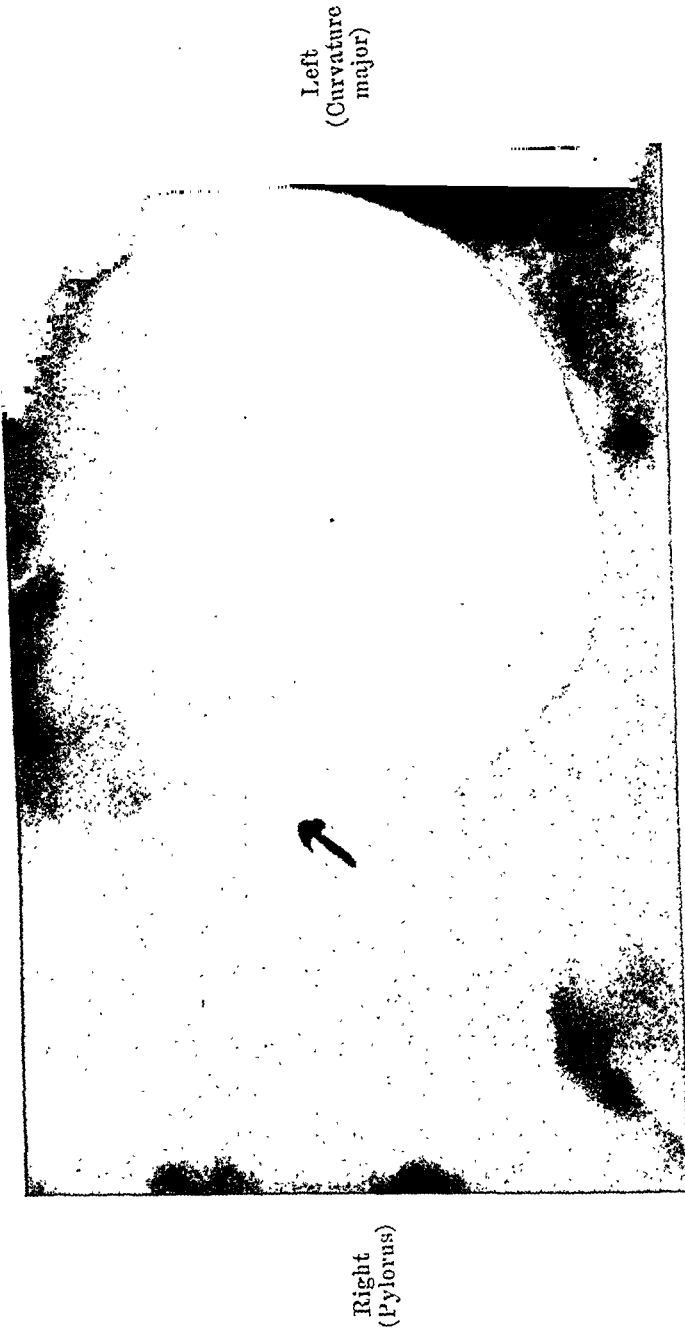
(III) The pseudoneoplastic, comprising, *inter alia*, dermoid cysts and blood cysts.

The most frequent of the benign tumours are the leiomyomas with 26.6 per cent (26). Fibromas are found in 4.5 per cent, and lipomas in 3.4 per cent. Both the epithelial and the mesenchymal tumours are often polypus, in which case the latter will frequently be solitary, in contrast with the former which are of multiple occurrence in many cases, in some in the form of a diffuse polyposis. In his publication MYHRE (29) states that the polypous form presumably occurs as a result of peristaltic action on the tumour, which, in contrast with the malignant tumours, does not infiltrate the wall.

A tumour of not infrequent occurrence is the so-called neurinoma. DJØRUP & OKKELS (11), FOG-MØLLER (14) and HARILD (15) have described cases of this tumour, which on closer histological examination prove to have originated from Schwann's syncytium. They display a motley morphological picture, as they undergo a cystic degeneration in many cases and may degenerate to become malignant. It is pointed out (11) that many of the cases previously described as sarcoma have presumably been neurinomas — or better: Schwannomas — at different phases of degeneration. It may moreover be mentioned that cases of neurinoma of the stomach have been described in Recklinghausen's disease.

Most frequently the benign tumours of the stomach, in particular the epithelial tumours, are small. In some cases they may assume monstrous forms; SCHARAPO (37) described a fibroma of 5,500 grammes, EUSTERMANN & SENTRY (13) a dermoid cyst of 1,000 grammes (in an 8-year-old boy).

The *etiology* of the benign tumours is unknown. RENANDER (34) points out that there is often a hereditary predisposition (according to WECHSELMANN about 50 to 60 per cent. of the cases). KONJETZNY quote (29) supposes that the epithelial polypi occur on the basis of a chronic gastritis and considers that achylia is always present in cases of benign tumour. Other authors, however, do not



X-ray picture of corpus et pars pylorica ventriculi. Barium in ulceration at →.

PAABY: Lipoma Submucosa Ventriculi Simulating Cancer.



support this theory, but achylia is at any rate of very frequent occurrence in the epithelial tumours. ASCHOFF quote (4), on the other hand, considers the gastritis to be secondary in relation to the polypi. DAERING quote (18) found inflammatory infiltration in all polypi of the stomach.

HARING (16), in a work on the connection between pernicious anaemia and polypous tumours of the stomach, demonstrated that from 10 to 14 per cent. of the patients with polypi of the stomach suffer from pernicious anaemia and stressed the importance of undertaking an examination of the blood in these patients as well as an X-ray examination of the stomach in all patients with pernicious anaemia. In another publication (3), 14 cases of polypus fibro-adenoma were reported, 3 of them being complicated with pernicious anaemia. In one of these cases the interesting fact was moreover observed that the pernicious anaemia subsided after resection of the stomach.

The *significance* of the benign tumours of the stomach is undoubtedly first and foremost their tendency to malignant degeneration. Especially the epithelial tumours involve the risk hereof. MILLER et al. quote (26) found malignant degeneration in 35 per cent., ACKMAN quote (26) in 15 per cent., BENEDICT & ALLEN quote (26) in 41.2 per cent., FORSMANN quote (14) in 12 to 60 per cent. HOLST (17) stressed correspondingly that epithelial tumours of the stomach should be considered a pre-cancerous disorder and that resection should be performed when this is suspected. It is pointed out in a single publication (24) that myomas quite often display sarcomatous degeneration, which applies in particular to the subserous myomas, whilst the submucous forms most frequently display cystic degeneration.

The tendency of the benign tumours to give *clinical symptoms* will, as a rule, depend on their size, as the great majority of the small tumours give no or only vague symptoms. The symptom of most frequent occurrence is anaemia, caused by haemorrhage. EUSTERMANN & SENTY (13) found haemorrhage in 37 per cent., JUDD & HOERNER (20) in 22 per cent. It occurs both in the epithelial and in the mesenchymal tumours and may be either manifest or occult. In many cases it originates — as in the case described here — from a large recess-like ulceration in the mucous membrane over the tumour, possibly passing into the tumour tissue. Such ulcerations, which may often attain a considerable size, occur chiefly in the large, mesenchymal tumours and may possibly



have been caused by an impaired nutrition of the mucous membrane distended over the tumour, in connection with the arrodging effect of the gastric juice, as achylia is not the rule in these tumours. BALFOUR & HENDERSON (3) found ulceration in 17 per cent., JUDD & HOERNER (20) in 32 per cent.

Another symptom of fairly frequent occurrence — and rather a characteristic one — is the *acute stenosis*. Such attacks, which occur most frequently in small stalky tumours localized near the pylorus, are due to the fact that through the peristaltic movements the tumour may close the pylorus, and may even in some cases be invaginated into it and slip into the duodenum, so that in a few cases it has been diagnosed radiologically as a duodenal polypus (19). The attacks are accompanied by colicky pain in the epigastrium and by heavy vomiting, they are most frequently transient and intermittent. They may in some cases simulate attacks of biliary colic (13). They may, however, also be seen in the case of tumours with a broader base. They will hardly ever occur in cancer of the stomach because this will infiltrate the wall, thus preventing the occurrence of the acute stenosis.

In other cases these tumours give rise to more chronic symptoms of stenosis. They have been seen in a few cases to produce ulcer-like symptoms, and EUSTERMANN & SENTY (13) point out that this applies in particular to the myomas situated near the pylorus. In this connection it may be mentioned that the attacks of stenosis mentioned above may in a few cases be so severe as to be suspected for a perforated ulcer (29). Lastly, many of the benign tumours are accompanied by more uncharacteristic, vague, dyspeptic symptoms, rather like those of gastritis, which applies in particular to the small epithelial tumours. In many cases they simulate cancer of the stomach.

It is thus quite a motley symptom picture which may be produced by these tumours — when they give any symptoms — and, consequently, the clinical diagnosis becomes difficult to establish. It may, however, be important to establish an early diagnosis because of the risk of malignant degeneration. In this connection it may be mentioned that primary sarcomas of the stomach, which, according to KAPEL (22), constitute 1 per cent. of all malignant tumours of the stomach (according to DJORUP & OKKELS (11), from 2 to 5 per cent.), may simulate benign tumours, as they often attain a considerable size without any signs of malignancy, in contrast with the carcinomas.

An important diagnostic aid is the *X-ray* examination, as the tumours often display characteristic signs here. It is difficult to diagnose radiologically the small polypous tumours, but in most cases they are best seen in examination of the mucous membrane with a small quantity of contrast medium and with compression. They will then appear in the form of scattered, roundish rarefactions. The following special characteristics are moreover seen: the tumour forms a well-defined defective filling, surrounded by a natural relief of mucous membrane. As a rule, peristalsis is normal; not so, however, if the tumour is ulcerated. Recesses are of fairly rare occurrence and are never associated with spasms. When a recess occurs — corresponding to an ulceration of the tumour — the usual convergence of folds of the mucous membrane will, as a rule, be absent, the recess will often be large, of a punched appearance, with smooth walls and without mounded edges. In the subserous, stalky tumours, a plug-shaped bulging of the contour at the basis of the stalk has moreover been described. Lastly, the defects are most frequently situated along the wall of the stomach, not involving the curvature.

BALFOUR & HENDERSON (3) reported 58 cases of benign tumour, 75 per cent. of which were X-rayed. 92.6 per cent. displayed a tumour and in 48 per cent. it was diagnosed as benign. It is thus difficult to decide the benignity of the tumour on the basis of the *X-ray* examination.

The *treatment* of benign tumours of the stomach will always be operative, partly because of the risk of malignant degeneration, partly because of the difficult diagnostics in connection with the often severe symptoms. This will, however, hardly apply to the multiple polypus tumours which assume the nature of a polyposis throughout the stomach and form part of a disorder of a similar nature also in the rest of the gastro-intestinal tract. Whether resection or excision should be chosen depends on the nature of the tumour. HOLST (17) and RIEGLER & ERICKSEN (35) recommend always to perform resection in tumours of epithelial appearance because of the great risk of malignant degeneration. In addition, they state that there is a risk of further dissemination to the stomach, even during the benign stage. Simple excision should thus undoubtedly be reserved for the larger, well-defined, solitary tumours which must be supposed not to be of epithelial origin and where such operation is otherwise technically possible.

## Summary.

The writer reports a case of large, submucous lipoma of the stomach, simulating cancer of the stomach. It was removed by resection. Mention is made of the frequency of benign tumours of the stomach and their classification. The etiology is discussed. The symptoms are gone over, the attacks of acute stenosis being stressed in particular. The risk of malignant degeneration and its importance to treatment are pointed out. Reference is made to the value of X-ray examination and to the characteristic X-ray findings. The treatment is operative; resection should be performed in cases of epithelial tumour.

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## **Cystectomy in the Male, the Significance of the Combined Prostat-Seminal Vesiculo- Cystectomy with Special Reference to the Sexual Function.**

By

RAGNAR ROMANUS.

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In 1887 BARDENHEUER performed the first total cystectomy for vesical cancer; the first successful cystectomy (for cancer in exstrophy) with implantation of the ureters in the intestine was made 1894 by the Swede BERGENHEM. This method of treatment has not, however, yet been generally accepted, and opinions as to its value still differ greatly, even among urologists. H. H. YOUNG (1926) "never felt justified in carrying out an operation of total cystectomy". Neither B. S. BARRINGER in his 34-page account of tumours of the bladder (Dean Lewis "Practice of Surgery" 1938), nor M. SÆGESSER (Spezielle chirurgische Therapie 1946) even mentions cystectomy. This is not because the cystectomy itself is a particularly extensive or difficult operation as compared to other cancer-operations, but because it is difficult to provide a vent for the urine which is safe, without unduly invaliding the patient. Especially since Coffey's experimental and clinical work, the uretero-intestinal methods of implantation have been used to an ever increasing extent. With modern control of fluid balance, chemo-therapy etc., the experience entitles us to consider the ureteral implantation according to Coffey's first method (*i. e.* open without catheter) as a valuable routine technique. It is a simple and safe procedure, it gives good primary results which also seem to stand the test of observation over a

longer period (see further HELLSTRÖM & ROMANUS 1947). The combined mortality after ureteral implantation in the intestine and total cystectomy has hitherto been high, because the method has been resorted to chiefly as a last resource in cases of extensive vesical cancer. In 1939 ORR, CARSON & NOVAK sent out a questionnaire to all American urologists, receiving 267 answers: among more than 26,000 cases of vesical tumour only 353 cystectomies had been performed by in all 68 surgeons. The mortality due to the cystectomy alone was evidently proportional to the experience of the operator; 18 surgeons who had operated in all 29 cases had 100 % mortality, while 16 surgeons with altogether 67 operated cases had a mortality of 50—100 %, 13 surgeons with 106 cases had 25—50 % mortality, and 21 surgeons with in all 151 cases had a mortality of only 0—25 %. The high mortality rate was considered to be due to the patients having been operated upon at a late stage, when metastases or more serious renal injuries had already developed, rather than to technical difficulties.

It is only in recent years, since the comparatively bad results of fulguration, resection and irradiation in the treatment of vesical cancer have been established, that cystectomy has been increasingly used. The operation has been resorted to at an earlier stage, and has also been used in connection with benign diseases such as extensive papillomatosis. This increased range of indications, as well as the relationship between the mortality and the experience of the operator, has been pointed out from the Mayo Clinic by PRIESTLEY & STROM (1943) and FERRIS & PRIESTLEY (1948): During the period 1910—1942 105 vesical carcinomas were operated upon, with a view to perform a total cystectomy, but only in 52 cases was it possible to remove the bladder. During the period 1937—1946, on the other hand, the operation was possible in 111 cases out of 119; and in the single year 1946 cystectomy was performed in 33 cases. In the period 1937—1941 the mortality was 25 %, but in 1941—1946, when one surgeon was responsible for the treatment of most of the cases, the mortality decreased to only 8 %; and the authors predict a further reduction. These figures may well be compared to the results obtained in other visceral cancers. This development towards greater radicality has in the Scandinavian countries been emphasized by HELLSTRÖM (1947, 1948) and STRÖMBECK (1948). The same tendency was met with at the meetings in The American Med. Assoc., Section for Urology in July 1946 (published as a Symposium on Urinary Vesical

Tumours in J. A. M. A., June 1947) and in the American Urolog. Assoc. in July 1947 (publ. in J. Urol., July 1948). I do not intend to discuss the indications for cystectomy.

With these extended indications, the technique for cystectomy, especially in the male, has also been increasingly taken up for discussion. The most common technique — and for the general surgeon also the most natural — was formerly the extraperitoneal loosening of the bladder from above with its separation from the rectum, in most cases also from the seminal vesicles, by means of blunt dissection, successive clamping of the vessels at the sides, and finally division of the urethra above or under the prostate. Probably on account of a natural aversion to removing normal organs, the majority of surgical manuals and textbooks recommend leaving the prostate and the seminal vesicles, which should be extirpated only when tumorous infiltration is present; *e. g.* ALBARRAN (1909), VOELCKER & WOSSIDLO (1921), MARION (1940), WEHNER (1942), ORR (1945). According to WARD (1936—37) and BEER (1937) as much of the prostate as possible should be left. In many accounts the seminal vesicles are not mentioned, and in the recent English urology (WINSBURY-WHITE 1948) the technique of cystectomy is not discussed at all. Even YOUNG (1926), however, pointed out that cancer of the bladder not infrequently involves the prostate, growing in the same manner as a primary prostatic cancer, producing enlargement, but not the same hard induration; S. WILHELM (1947) makes the same statement. In a great survey of total cystectomy HINMAN & SMITH (1939) write: "If the cancer involves only the lateral or posterior wall of the bladder without affecting the prostate or seminal vesicles, cystectomy may be all that is necessary, although it has been proved that the limits of malignant growths cannot be ascertained by inspection. Microscopically isolated islands of cancer cells may be found far removed from the primary growth. In most instances, therefore, complete prostato-seminal-vesiculectomy is indicated, it becomes necessary when the prostate is the site of primary cancer or is secondarily invaded by tumour. We have always planned radical excision of the prostate and seminal vesicles along with the bladder in men." PRIESTLEY & STROM (1943) always remove the prostate and the seminal vesicles after they had observed 2 local recurrences of vesical cancer in the prostatic urethra; they point out that cancer in the trigone sometimes involves the prostate. In 2 of their 105 cases besides the vesical

cancer an independent tumour was revealed in the prostate. DEAN (1948) "removes the prostate with the bladder, because we have observed, as have others, that infiltrating tumours of the bladder base sometimes invade the prostate, and when the bladder is the site of papillary tumours, the prostatic urethra either is affected with the bladder or shows the earliest recurrences after the bladder has been removed". Thus, especially in recent years, the development has been clearly in favour of increasing local radicality, with removal of both the prostate and the seminal vesicles, especially in writers with an extensive material of their own. However, this has been partly for technical reasons, as more and more surgeons have abandoned the "natural" method with successive loosening from above for a "retropubic" technique starting with division of the urethra below the prostate (HARRIS 1902, COFFEY 1933, HINMAN 1935, MILLIN 1947), or a combined perineo-abdominal operation (ALBARRAN 1909, G. G. SMITH 1935, EWERT 1947, MARSHALL 1947, RITTER 1947, WILHELM 1947, DEAN 1948) or an abdomino-perineal procedure (KÜSTER 1891, BEER 1937, HINMAN & SMITH 1939, DODSON 1944, STRÖMBECK 1948). WILHELM states (1947): "The suprapubic abdominal operation has failed too often in men because of incomplete prostatotomy, leaving a stump of prostate and urethra, which is the site of residual neoplasm." MARSHALL (1947) has observed at least one instance of recurrence in a small bit of prostate which had been left. DEAN (1948) "believes, that in most cases a cleaner and more complete removal can be performed through the two approaches (*e. g.* perineo-abdominal). We know, however, that the entire bladder and prostate can be removed through the suprapubic approach and the time saved in this way may be a favorable factor." The surgeons of the Mayo Clinic, however, still use the suprapubic method. FERRIS & PRIESTLEY write (1948): "It appears to us that as radical removal of the bladder (with the seminal vesicles, all of the prostate gland and 2 to 3 cm of the urethra beyond the tip of the prostate) can be accomplished through the suprapubic approach alone as if perineal exposure in addition were used."

Complications other than insufficient radicality as a consequence of the leaving of the seminal vesicles and the prostate wholly or in part intact are very seldom discussed in the literature. BEER (1937) who routinely divides the prostate in the middle and sometimes introduces radium needles into the cut surface of

the prostate, has in some cases observed prolonged wound-discharge, probably due to necrosis of the prostate. No author discusses the disadvantages of the more radical procedure with removal of the prostate and the seminal vesicles in every case of vesical cancer in men. Only WARD (1936—37) mentions one patient with a normal sexual function after the operation; in this case the prostate was divided well above the verumontanum (colliculus seminalis), and both the seminal vesicles and their openings into the urethra were preserved. The sexual function in W's other 5 patients is not mentioned, however; in these cases the prostate was cut more distally or the whole prostate — with the seminal vesicles — was extirpated. COFFEY (1933) in passing mentions a case of post-operative impotence in a man with prostatic cancer in which both the prostate, the bladder and the seminal vesicles were removed. Other publications, however, say nothing concerning the sexual functions in men after cystectomy.

The disadvantages of the operative removal of the prostate and the seminal vesicles are, on the other hand, discussed by several writers in connection with total prostatectomy and vesiculectomy when these operations are not combined with a cystectomy. YOUNG (1937) writes that "the prostate plays a very important part in urination, coitus and ejaculation", and (1926) that the patients "may have fairly satisfactory coitus, generally only slightly impaired" after the removal of the seminal vesicles and the ampullae even if the lateral prostatic lobes have been removed (for tuberculosis). LOWSLEY & KIRWIN (1944) consider that an ejaculation is out of the question — "which is very distressing to the patient" — if the ejaculatory ducts are removed in connection with a total prostatectomy; also a vesiculectomy is frequently followed by a period of impotence which usually lasts for 2—3 months, but rarely may be permanent. GUTIERREZ (1942), on the other hand, who has performed more than 150 vesiculectomies, says that after this operation "the sexual potency remained apparently unchanged in most instances". It is a well-known fact that perineal prostatic operations often entail impaired potency. To quote HENLINE (1947): "Impotence may very frequently result from perineal surgery, regardless of the type", and MILLIN (1947): "The frequency with which sexual impotence follows a perineal prostatectomy is well known." In ORMOND's material (1947), comprising 29 radically perineally operated prostatic cancers, only one patient, a 48-year-old man, was able to have an



erection after the operation. In experiments on animals STEINACH showed as early as 1894 that the loss of the seminal vesicles does not diminish the potency (though the fertility, on the other hand, is affected). These results were confirmed by WALKER (1911) and STRAUSS (1924), who besides the seminal vesicles removed the greater part of the prostate.

As regards the sexual function, it may further be pointed out that according to many sexologists, *e. g.* van DE VELDE (1932), the orgasm takes place when the semen strikes the urethral wall in a fine jet. EISENDRATH & ROLNICK (1938) write: "Removal of the seminal vesicles results in impotence. The pleasurable sensation at the height of orgasm is due to the passage and squeezing of the semen through the ejaculatory ducts." KINSEY, POMEROY & MARTIN (1948), on the other hand, consider that "orgasm may occur without the emission of semen".

The statement that the prostate has an endocrine function and that, consequently, a total removal may entail certain impairments must now be considered to be entirely disproved.

### Author's Material.

During the period 1940—1947, 49 cystectomies have been performed on male patients at the Surgical Clinic of "Karolinska sjukhuset". In recent years the indications have been more and more extended, and cystectomy has been performed in cases of non-malignant but extensive papillomatosis of the bladder (8 cases) and severe chronic cystitis with contracted bladder (3 cases, one of which, however, had been diagnosed preoperatively as a cancer, and another as a papilloma), and further, in early stages of vesical cancer in comparatively young men, for whom the sexual function still plays a great rôle (altogether 38 cases of vesical cancer and malignant papilloma). Among these 49 patients the prostate was extirpated in 29 cases, in 28 of which the seminal vesicles were also removed. In 4 of the 20 other cases the prostate was cut approximately in the middle, while it was left largely intact in 16; in only 5 of these cases, however, was it left quite untouched, while in the remaining 11 cases the division was made through the upper part of the prostate, or the first part of the urethra was cauterized. Being rather heterogeneous the material may help to solve the question as to whether the prostate and the seminal vesicles ought to be removed or left intact in connection

with a cystectomy. An analysis has therefore been made of the indications, the radicality of the operation and the complications in the 49 cases. Data concerning the sexual function during a shorter or longer period after the operation have also been obtained from 21 of the patients.

During the first years of the period covered by this report, the prostate and the seminal vesicles were routinely left intact in cystectomy. They were removed only if pronounced adhesions were found with fixation of the bladder to the seminal vesicles and an extravescical extension was suspected. The prostate was, as a rule, removed in cases of tumour in the neck of the bladder with extension to the prostate and in cases in which changes giving rise to the suspicion of malignancy were observed in the prostate before or during the operation. The indications for removal of the prostate and the seminal vesicles have not been so strictly limited in recent years, and these organs have sometimes been removed chiefly for technical reasons. The technique has been extra-peritoneal blunt dissection of the bladder from above towards the base with successive ligation of the vessels. In the first part of the period here dealt with, it was attempted to leave as much as possible of the prostate, and the division was frequently made through the prostatic gland tissue. The nearest part of the urethral mucous membrane was cauterized and if possible closed with sutures. This successive blunt dissection of the prostate in the bottom of a deep wound is difficult, and the tip of the prostate has in some cases been left behind even when it had been planned to remove the entire prostate and cut the urethra distal to the apex; *i. e.* the division has as a matter of fact been made through the parenchyma. From anatomical descriptions and from autopsy studies made by the author it is obvious that the apex of the prostate is fixed to the symphysis by means of the pubo-prostatic ligament and to the urogenital diaphragm. It is only when it has been loosened from these connections that it can be drawn up and the membranous urethra be stretched, leaving room for a clamp. A study of the operation reports and of the descriptions of the specimens as well as a comparison of the findings on post-operative palpation makes it probable that the prostatic tip has been left in 7 cases. The same possibly holds good for a further 7 cases. The division was made approximately in the middle of the prostate in 7 other cases; in 3 of these, however, the rest of the gland was removed secondarily during the operation. In 2 of the

cases the removal was performed on account of chronic prostatitis, while in the third case the division showed that the prostatic urethra was filled with papillomatous tumour masses; the secondarily removed part of the prostate showed foci of (papillomatous) cancer.

In the evaluation of the *radicality* of the operation 3 cases of chronic cystitis with contracted bladder have to be ruled out. Of 8 cases of benign papilloma the prostate and the seminal vesicles were removed in 3 and left intact in 5. In one of these cases a papilloma was present around the inner urethral orifice, for which reason the mucous membrane was cauterized here on operation. The radicality cannot be considered quite certain in this case, but the patient is still free of symptoms more than one year after the operation.<sup>1</sup> Among the 38 cancers of the bladder (including malignant papillomas), one showed at operation such a marked perivesical extension of the tumour that a radical removal was impossible and only a palliative cystectomy was carried out (the prostate and the seminal vesicles were left intact). The operation was definitely, or probably, radical in 15 cases. 10 of these patients are still living; the prostate was removed but the seminal vesicles left in one of these cases, while in the remaining 9 both the prostate and the seminal vesicles were removed. 5 patients died without signs of persisting tumour or metastases; in one of these cases the prostate and the seminal vesicles were left while they were removed in the other cases.

The operation had probably not been locally sufficiently radical in 9 cases, cancer tissue possibly being left, in 7 cases in the prostate, in 2 cases in the seminal vesicles. Furthermore, in all these cases, with 3 exceptions, cancer cells were demonstrated in the operative specimen in the lymph or blood vessels or outside the bladder. The result would perhaps have been the same — *i. e.* local relapse or metastases — even if the prostate and the seminal vesicles had been completely removed.

In 2 cases the cancer grew up to or into the vesical orifice; in these 2 cases the urethral mucous membrane was cauterized but the prostate left; in 3 cases the vesical cancer infiltrated into the prostate, which was removed to a greater or lesser extent, it is, however, not certain that all the tumour tissue had been eradicated; in 2 cases there was a prostatic carcinoma besides the vesical neoplasm, one of these only showed roentgenologically demonstrable changes giving rise to the

<sup>1</sup> 1 1/2 years after the operation this patient got urethral bleeding from papillomas, necessitating successive extirpation of the whole remaining urethra.

suspicion of cancer in the prostate, which was left intact; in the other case several foci of primary prostatic cancer were found in the removed prostate, including one in the lower resection-edge just adjacent to the prostatic apex; in 2 cases the cancer infiltrated the entire vesical wall reaching into the perivesical tissue in the region of one of the seminal vesicles, which had been left.

In still another case a recurrence had occurred, probably because the prostate had not been primarily extirpated. In a case of papillomatous vesical cancer the intention was to remove the entire prostate, which was loosened from above and clamped distally; owing to insufficient exposure of the prostatic apex the clamp did not grip the membranous urethra but the prostate itself, and slipped off after the division. A large amount of tumorous tissue thus poured into the wound, and the patient died one month after the operation with an extensive local recurrence.

In 8 cases, judging from the post-operative course, the operation was not radical, despite the complete removal of both the prostate and the seminal vesicles. In the remaining 4 cases the operation was not radical either; this was, however, probably not due to the fact that the seminal vesicles or the prostate — or part of it — was left; as in no case was cancer tissue demonstrable in the region of these remaining organs. In 3 of the cases, however, cancer cells could be demonstrated in the operative specimen outside the bladder wall or in the lymph vessels. Therefore insufficient local radicality, leaving the prostate and the seminal vesicles, was certainly not the cause of the continued spreading of the cancer or of death.

*Microscopic examination* of the removed organs has not been carried out in all cases; but 8 specimens presented benign hypertrophic changes in the prostate. In 5 specimens a chronic prostatitis was demonstrated and in 6 cases cancer was revealed in the prostate. In 2 of these 6 cases this finding came as a complete surprise; one concerned a 62-year-old man with vesical cancer and a clinically demonstrable benign moderate hypertrophy of the prostate; a primary prostatic cancer was found in several places, among others in the lower resection surface through the apex (see above). The other case had a cancer in the anterior part of the bladder. Microscopic examination revealed infiltration of the vesical cancer in the prostate, which clinically had presented only moderate benign enlargement. — In both these cases the cancer in the prostate had not given rise to any symptoms before

the operation, and the removal of the prostate was here chiefly due to the recent, more liberal, attitude towards extirpation. In the other 4 cases the finding of vesical cancer infiltrating also the prostate was not quite so surprising in view of the basal localization of the carcinoma. 3 of 4 patients showed on the urethrocytogram definite or suspected changes in the prostatic part and 3 (2 of these and the fourth) showed on palpation of the prostate a certain asymmetry and some increase of the consistency (though not typical cancerous induration)..

A number of *complications* have occurred in more or less definite relation to the type of operation performed: Most important is the above-mentioned slipping off of the clamp owing to division *through* the prostate instead of distal to the apex. In one case of papillomatous vesical cancer the division was made through the prostate, but as the urethra was filled with tumour masses, which had also infiltrated the prostate, this gland had to be entirely removed (see above). This patient returned 3½ months after the operation with a retropubic abscess, which had spontaneously perforated the scar. He subsequently got a rectal fistula and died 8½ months after the operation from metastases of the lymph nodes and lungs, without any local recurrence. In this case, however, the issue is probably to be ascribed to primary spreading of the tumour, and not to the operation. It is possible, however, that the technique employed was to a certain degree responsible for the occurrence of the cavity.

On 2 occasions *fistulas or cavities* have arisen which were possibly connected with necrosis of remaining prostatic tissue.

In the one case, where the fistula still existed 18 months after the operation, the division through the prostate was made with diathermy, but the patient had also received intensive irradiation. In the other case, the autopsy 8 months after the operation (cause of death: diabetic coma and uremia) showed an abscess cavity at the site of the bladder — the entire prostate had been left, and the urethral mucous membrane had been cauterized.

The *drainage* may of course play a certain rôle in the occurrence of the last-mentioned complications. As a rule, a couple of cigarette drains + a coarse rubber tube, sometimes a Mikulicz bag, have been used suprapubically. On 3 occasions the operative cavity has also been drained with a catheter in the urethra (as recommended by HINMAN 1935, PRIESTLEY & STROM 1943). The period required for healing has not always been recorded, but in the majority of the other cases it was longer than in these 3.

In another case, scarcely 3 weeks after the operation, there was a spontaneous discharge from the wound through the urethra after which secretion from the wound rapidly diminished. In a further 2 cases some time after the patients had returned home there was a urethral discharge, which soon ceased spontaneously. This had probably arisen in the same way, through secondary emptying into the urethra. In one of the above-mentioned cases — where the prostate was divided before extirpation — a perforation of the retropubic cavity to the rectum occurred without definite local recurrence. It is possible that this complication might have been avoided by urethral drainage. In 2 further cases a fistula or a cavity was present postoperatively; in one of these a perforation to the rectum occurred secondarily. These complications were, however, caused by a recurrence of the cancer, for which reason the cases are not suitable for an estimation of the value of the different procedures in surgical technique and drainage.

The material does not permit of any definitive conclusion as far as the most suitable form of drainage is concerned, but it would seem to be well worth while to try urethral drainage in more cases.

If the urethra is cauterized on a level with the verumontanum or the prostate is divided distal hereto, the ejaculatory ducts will be obstructed. This will give rise to a stagnation in efferent sperm-passages and the possibility of an infection in this system. In 3 cases *epididymitis* has arisen after the operation.

In one of these the prostate was entirely removed; but even before the operation the patient had symptoms from the side on which the epididymitis appeared one month after the operation. He died 5 months later with metastatic pains on the same side. — The connection between the epididymitis and the operation itself seems uncertain in this case. In the other two cases the division had been made through the prostate. In one of these an epididymitis and vesiculitis occurred on one side 6 weeks after the operation, while the other seminal vesicle was infiltrated with cancer. In the other case the patient had a chronic prostatitis, and during the operation the vas deferens on one side was broken off. Two months later he had a funiculitis and epididymitis on the other side. 18 months after the operation he is suffering from increasing discomfort and has discharge, urethral hemorrhage and pains on ejaculation — caused by a *chronic prostates-vesiculitis* and a urethral stricture. Another patient, who had not had any prostatic trouble before the operation got slight subjective and objective symptoms of *prostates-vesiculitis* 3 years later. 5 years after the operation these symptoms increased, rendering the patient completely incapable of work (besides inhibiting his sexual function — see below). On the other hand, a 58-year-old patient with vesical cancer who before the operation had shown clinical signs of acute prostatitis has been free of symptoms for 22 months after the operation, although half of the prostate was

left. A 34-year-old patient with a contracted bladder, urethral strictures and a palpable prostatitis with roentgenologically demonstrable cavities, had only the bladder removed, while the prostate and the seminal vesicles were left intact.  $3\frac{1}{2}$  years after the operation he still has objective signs of prostatitis, though he has no subjective discomfort and enjoys a normal sexual function with proven fertility (see below). A 40-year-old man with chronic cystitis and contracted bladder suffered before the operation from a discharge and right-sided epididymitis; at operation, however, both the prostate and the seminal vesicles felt normal and were left intact. It is not yet possible to appraise the development in this case, as the operation was only recently performed.

A further *complication* occurred in connection with the operation, viz., a *rectal injury* when dividing the membranous part with diathermy. It is not, however, possible to ascribe this injury to the radical extirpation itself (including the prostate and the seminal vesicles). The left-sided bladder tumour seemed to have infiltrated the left seminal vesicle, and the left prostatic lobe was on rectal palpation found to be very hard, for which reason these organs also had to be removed (microscopic examination incomplete). The rectal lesion was sutured but it ruptured secondarily and the patient died of cachexia 2 months after the operation. The autopsy showed no cancer in the pelvis.

Data concerning the *sexual function before and after extirpation of the bladder* have been obtained from 21 patients, comprising 10 in whom the prostate and the seminal vesicles were left, 4 in whom the seminal vesicles were left while the prostate had been partially removed (with blocking of the ejaculatory ducts as the probable result), and 7 in whom the prostate and the seminal vesicles were completely removed.

Cases in which the prostate and the vesicles were left intact: The material comprises 10 cases: 3 with vesical cancer, one with malignant papilloma, 5 with multiple benign papillomas and one with a chronic cystitis with contracted bladder. Five of the patients, aged 34, 40, 43, 44, 47 years at the time of operation, enjoyed entirely normal sexual function before and after the operation. Besides these, one patient aged 45 years had a slight depression of the libido after the operation, though it has been improving during the later part of the observation-period (one year). Another patient, aged 52 years, had normal functions during the first years but ceased all sexual intercourse nearly 5 years after the operation on account of pronounced prostatic-vesiculitis with pains in connection with ejaculation (see above). One patient, aged 55 years, who has been under observation for 18 months, has reduced libido, normal erection, but he has not had coitus on account of wife's illness; there have been no pollutions either. In a 72-year-old man with

malignant papilloma all sexual manifestations had ceased even before the operation. In a 64-year-old man with vesical cancer the urethra had been cauterized at operation. He suffered from reduced potency for 18 months after the operation; he had attempted coitus without success. The patient died of his cancer 3 years after the operation. Two of those who now have normal functions state that these were clearly impaired during the first period after the operation with complete or partial impotence, which is probably rather common after such extensive surgery, frequently followed by irradiation. It is further a striking feature that the man with chronic cystitis, aged 34 years at the time of operation — now 38 — is definitely fertile, as his wife gave birth to a boy 2 years after the operation, and this despite the fact that a prostatitis as well as several urethral strictures had been diagnosed before the operation (see above).

Thus, of these 10 patients with intact prostate and seminal vesicles 7 enjoy unchanged sexual function after the operation (after a temporary impairment in at least 2 cases). In 3 patients, however, the function has been impaired; in 2 in direct relation to the operation and in one secondarily through a subsequently occurring prostatic-vesiculitis about 5 years post-operatively.

Cases in which the seminal vesicles were left intact, while the prostate was partially removed: The material comprises 4 cases of vesical cancer (45, 50, 58, 60 years of age). 2 patients had *unchanged* sexual functions after the operation except that the amount of semen was small and the fluid ejaculated almost as thin as water. The semen doubtless consisted only of prostatic secretion in an amount roughly corresponding to the size of the remaining part of the prostate (estimated by rectal palpation) as no secretion can pass from the testes, epididymides and seminal vesicles on account of obstruction of the ejaculatory ducts. A 60-year-old patient, who had ceased having coitus 18 months before the operation, died 3 months later. During the first period after the operation the 50-year-old man enjoyed a normal sexual function with a small amount of semen; but now, one year later, he has voluntarily stopped having coitus on account of painful ejaculation due to prostatic-vesiculitis and urethral stricture (see above). This patient's sexual function has thus been impaired after the operation.

The last and most interesting group comprises 7 patients in whom both the seminal vesicles and the prostate were removed.

One 51-year-old man with benign papillomas for 2½ years after the operation enjoyed unchanged sexual functions except that he had



no ejaculation at all, though coitus and orgasm were the same as preoperatively. At that time he began to grow weaker in this respect — libido and potency disappeared —; this proved, however, to be due to metastases in the vertebrae and lungs, probably from a primary tumour in the hilum. The patient died 2 years and 9 months after the operation. A 57-year-old man with vesical cancer often during the night has normal erection which is somewhat weakened in an otherwise normal intercourse with orgasm though without ejaculation. Libido is also somewhat reduced, but is growing stronger. The patient is a chronic alcoholic, with a somewhat impaired renal function since the operation (NPN exceeds 50 mg%) and a considerable secondary anemia (Hgl. 58 %).

A 64-year-old man who had received irradiation for suspected vesical cancer, though no cancer could be observed in the extirpated bladder, had during the first period after his discharge nightly erections a couple of times but no coitus. The patient then began to grow weaker while at the same time he developed icterus. He died 7 months after the operation in hepatic coma. A 66-year-old man with vesical cancer during the first period following the operation had normal libido, which later gradually disappeared. The whole time (followed over 5½ years after the operation) he has been completely impotent. Both libido and potency disappeared entirely after the operation in the 3 other patients, though this may have been at least in part due to other causes than the loss of the prostate and the seminal vesicles: 1) A 62-year-old man operated upon for malignant papillomas of the bladder and prostatic cancer (radicality doubtful) is still, one year after the operation, suffering from impaired general condition and a considerably affected renal function with NPN at times about 100 mg%. 2) A 60-year-old man, who had 2 years previously been operated upon (trans-vesical prostatectomy), and had received intensive irradiation, is still, 18 months after the operation for vesical cancer, in a rather poor general condition with persistent suprapubic fistula, urethral discharge and possible recurrence. 3) A 67-year-old man with irradiated vesical cancer had 9 months after the operation a somewhat affected renal function with NPN 50 mg%.

Thus, of the 7 patients in whom the prostate and the seminal vesicles were removed 2 had unchanged, or only slightly impaired, sexual function after the operation (apart from the fact that there has been no ejaculation); one had at first normal erection but soon died from another disease; 3 patients had inhibited functions after the operation, which in at least 2 cases may be ascribed to the primary disease and its complications without direct relation to the type of surgery; one patient had for a period following the operation a normal libido but was impotent, which is presumably a consequence of the operation. The dissection was difficult in this case; the prostate and the seminal vesicles were

removed with diathermy, and the possibility of nerve-injury must be taken into consideration. In this case, however, there was also a contributory factor, as before the cystectomy the patient had received intensive irradiation on the exposed and opened bladder.<sup>1</sup>

### Discussion.

The experiences from these cases thus reveal that in adult men potency and normal *orgasm* are not dependent upon the presence of the prostate and the seminal vesicles, and that the ejaculation is not necessary for the orgasm. Observations on other patients also show that it is erroneous to consider the orgasm to be released by the passage of the sperm through the ejaculatory ducts or by the impact of the jet of the sperm on the anterior urethral wall. One of these patients, a 32-year-old man with congenital atresia of the openings of the ejaculatory ducts has orgasm, which he describes in an adequate manner although he has no ejaculation (the amount of prostatic secretion is very slight). In another patient, a 37-year-old man, with congenital exstrophy of the bladder the ejaculatory ducts open upon the exposed verumontanum, the anterior wall of the bladder and the urethra being entirely absent. After a minor operation on the malformed penis he is able to have coitus. On ejaculation the sperm slowly flows out of the openings of the ejaculatory ducts but he states that he has orgasm as this is usually understood.

*The disturbances of the sexual function* which have been described in connection with operations on the prostate and the seminal vesicles — perineal, total prostatectomy, perineal vesiculectomy — must consequently not be ascribed solely to the removal of these organs. Similar changes, with impaired potency, deficient orgasm, and interference with ejaculation sometimes appear after abdomino-perineal extirpation of the rectum and after operations upon the sympathetic nervous system. The disturbances should therefore more probably be ascribed to nerve-injuries sustained in connection with the operation than to the loss of the organs themselves. In an uncomplicated abdominal cystectomy, with removal of the prostate and the seminal vesicles, the dissection

<sup>1</sup> In addition, it may be mentioned that it was impossible on examination to show any differences between patients with and without prostate and seminal vesicles in respect of physical and psychic condition, blood status with differential count and palpation of the testes.

of the organs is chiefly made bluntly in the prevesical space of Retzius and its continuation. By this procedure only the peripheral nerves and ganglia — situated close to the organs — are removed while the nerve-plexuses are left uninjured. Only in cases of severe inflammatory changes or perivesical extension of the tumour is there a risk of going outside this "cleavage" and causing nerve-injuries. Also an intensive preoperative irradiation may render the operation difficult in this respect. It is, on the other hand, considerably more difficult entirely to avoid nerve-injury, in perineal operations as well as in connection with difficult rectum extirpation. These injuries are often of a temporary nature, but they may be permanent.

Further, post-operative sexual disturbances may of course be due to psychic factors, functional disturbances in other organs, impaired general condition and so forth. Not infrequently, simply a long stay in hospital, convalescence, weakening irradiation etc. may entail such a prolonged interruption of sexual intercourse that elderly persons after regaining their health do not resume sex relations even if these were regular before the treatment. For many patients, both middle-aged and elderly, normal sex function is, however, a vital factor. This is ignored both by themselves and by the doctors, or is overlooked in the acute stage when the treatment must aim at saving life and health; but when the patients are restored to health it reasserts itself. This factor thus deserves closer attention than has hitherto been bestowed upon it when planning the treatment, and the value of our different methods of treatment need to be examined and discussed also from this point of view.

On the basis of the present material it is not possible to judge whether the risk of sexual disturbances after cystectomy is greater in connection with removal of the prostate and the seminal vesicles than it is, if these organs are left intact. The material is not extensive enough, and it has been selected on the principle that chiefly the most severe cases — in which adhesions have existed, perivesical extension of the tumour has been suspected and so on — have been subjected to a prostato-vesiculectomy; in addition, most of these patients have had a comparatively poor general condition and impaired renal function.

On studying the material from the point of view of *radicality and complications* it is worth while pointing out the following facts concerning the choice of surgery — whether the prostate

and the seminal vesicles should be removed or left: 1) The localization and extent of the tumour: According to larger surveys, about  $\frac{3}{4}$  of all cases of vesical tumours are localized to the base of the bladder, and this applies to an even greater number of the cystectomy-cases. It is important that all the possibilities of determining the extent of the tumour and its involvement if any, of the prostate and the urethra should be exhausted before the operation. Especially bimanual rectal palpation — preferably under anaesthesia —, endoscopy and X-ray examination with urethro-cystography, including micturition pictures, should be performed. But cases do occur in which all the findings are negative even at operation, and despite this fact microscopy reveals growth of vesical cancer in the prostate. In altogether 5 cases a vesical cancer was shown to involve the prostate, often far distally, for which reason it was necessary to remove the entire gland, including the apex, in order to ensure radicality. Extension to the seminal vesicles does not occur frequently, but it may exist without definite signs at operation. In these cases the leaving of the seminal vesicles entails local recurrence (2 patients). When the tumour is localized to the base of the bladder the radicality should be ensured by complete removal of the prostate and the seminal vesicles independently of the preoperative findings.

2) Other changes in the prostate and the seminal vesicles. Above all should be mentioned the not infrequent occurrence of primary prostatic cancer among older patients and the impossibility of revealing the malignancy preoperatively (one surprising case). The prostatic cancer is often situated in the caudal, dorsal part, for which reason the removal of the whole prostate, including the apex, is necessary. Ordinary hypertrophic changes of a moderate extent do not constitute an indication for prostatectomy, but they may conceal a cancer (see above). In cases of chronic prostatitis the possibility of a later aggravation of the condition should be taken into consideration; this occurred in 2 cases, 1 and 5 years respectively after operation. An inhibition of the sexual functions and even inability to work may be a consequence hereof. In one of the two cases mentioned no signs of prostatitis had been revealed before the operation. When the surgical procedure is planned, the patient's age and the desirability of retaining his fertility must be taken into consideration.

3) Risk of complications; technique. When performing a cystectomy it is scarcely more difficult, technically, to remove the prostate and the seminal vesicles than to leave them; not infrequently it is even easier. When loosening from above, it is necessary to be especially careful to free the apex of the prostate properly from its attachment to the urogenital diaphragm and to the symphysis, as a remnant, which may jeopardize the radicality and give rise to complications, may otherwise easily be left. A division of the prostate (as recommended by WARD and BEER) has been performed several times. This method, however, entails the risk of complications, such as the slipping off of the clamp on the stump and leakage of the content of the bladder into the operational area, as well as necrosis of the surface of the prostate (especially if it is cut with diathermy or pricked with radium needles as BEER recommends), with prolonged wound secretion and persistent fistula as a possible consequence. This technique has no advantages over the total removal of the prostate, as the ejaculatory ducts are as a rule obstructed, especially when the urethral mucous membrane has been cauterized from the cut surface. An obstruction of the ejaculatory ducts or the leaving of the seminal vesicles when the prostate is removed, entails the risk of vesiculitis and epididymitis, which occurred in 2 cases. In one of these cases a vesiculitis and epididymitis appeared on the one side, but not on the other, where the vas deferens had been broken off during the operation. A rectal lesion arose through the extirpation of the prostate and the seminal vesicles in one case. Here, however, the extirpation was necessitated by tumour infiltration, which rendered the loosening especially difficult. In ordinary cases it is probably not necessary to divide the urethra with diathermy, which increases the risk of injuring the rectum. The risk of rectal injury is, of course, the chief threat throughout the operation. WARD, for instance, speaks of "the fear of tearing a hole in the rectal wall being constantly present". As MARSHALL emphasizes, this risk is less pronounced when the combined abdomino-perineal or perineo-abdominal method is employed; but, as has been already pointed out, the risk of disturbances of the sexual function is considerable in all perineal operations. According to EWERT, "in some of the patients leakage of the urine per rectum has been noted after the perineal approach"; and MARSHALL, too, reports 3 cases with rectal insufficiency after the perineal method. The troublesome and dangerous loosening of the

prostate may be facilitated, if the operation, after suprapubic incision, is started retropubically with the division of the urethra, followed by the loosening of the prostate and the seminal vesicles with the bladder en bloc from below and upwards from the rectum — according to HARRIS, COFFEY, HINMAN and MILLIN. At “Karlinska sjukhuset” attempts are being made to modify this method, retaining its advantages and avoiding the drawbacks, especially the troublesome bleeding from the prostatic plexus, which caused HINMAN to abandon the method.

The planning of the operation requires a careful *sexual anamnesis*. In patients whose sexual functions have stopped there is no reason for leaving the prostate and the seminal vesicles. A number of these patients have voluntarily renounced the begetting of children; in other cases the marriage is primarily or secondarily sterile. In somewhat younger patients, on the other hand, it may be desirable to retain fertility. In some cases an examination of the semen may be performed preoperatively, in order to make it possible to discuss different alternatives before planning the operation. In all cases of vesical cancer and papillomas in older men, however, the question of radicality should be decisive, and the entire prostate as well as the seminal vesicles be removed with the bladder.

### Summary.

The experience from 49 extirpations of the bladder in the male shows that fewer complications, both immediate and late, occur in the 28 cases in which the prostate and the seminal vesicles were removed than in those in which they were left. It is impossible — despite careful preoperative examination with urethro-cystography and endoscopy as well as palpation before and during the operation — definitely to exclude pathological changes in the seminal vesicles and the prostate. For this reason the radicality of the operation will often be questionable when these organs are left. The experiences from 21 patients who describe their sexual function after extirpation of the bladder show that, despite the removal of both the prostate and the seminal vesicles, the *potentia coeundi* may be normal, *i. e.* the erection normal, the course of the coitus normal, ending in a normal orgasm but of course without ejaculation. As secondary complications may arise from apparently normal seminal vesicles and prostate left

behind at operation, these organs should on principle be removed in all cases of malignant vesical tumour. Only in cases of clearly benign changes in patients for whom it is particularly desirable to retain fertility should the leaving of the prostate and the seminal vesicles be considered.

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## **Gelatine and Polythene Film as Dura Substitutes and Polythene Plates as Bone Substitute in Skull Defects.**

By

EDUARD BUSCH, JENS BING and E. HART HANSEN.

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As part of the extensive investigations into the subject of the plasma-protein fractions in the blood, started in the United States during the war, there appeared a work by FERRY & MORRISON who had produced some fibrine preparations. These included fibrine film, made from fibrine by a special method resulting in a pliable and elastic substance whose absorbability could be altered by means of variations in the technique of manufacture (MORRISON & SINGER). This fibrine film was employed by INGRAHAM & BAILEY as a substitute for the dura mater, first on monkeys and later on patients, whereby it was proved that in fibrine film a substitute had been found that was preferable to earlier substitutes consisting of fascia lata transplantata, gutta percha, rubber or metal. There was no adherence between the fibrine film and the surrounding tissues, and while the film was slowly absorbed, a new membrane of connective tissue formed, covering the defect and peripherally growing together with the normal dura mater.

However, fibrine film being difficult to procure, it would be desirable if other suitable substitutes could be found. In the following an account will be given of the results of experiments with gelatine and polythene films, and also of some experiments on the practicability of polythene plates as a bone substitute.

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### Gelatine Film.

The gelatine film employed<sup>1</sup> was manufactured from formalin-hardened gelatine to which had been added sulphonated lauryl-alcohol to make the film more flexible and easier to stitch. It had been found in earlier, tentative experiments that films prepared in this manner were only slowly absorbed after being placed intraperitoneally in rats, where the film was still to be seen a month after insertion. It was found with the microscope that the gelatine, which was caught by the omentum, was surrounded by a narrow border of leucocytes and mononuclear cells and a moderate connective-tissue reaction (BING).

After being inserted intrapleurally into two rats the film was found to have been absorbed, without adherence formations, in  $3\frac{1}{2}$  weeks, and thereafter the question was examined of whether or not this gelatine film was suitable as a dura substitute. This was tested on four cats, which were trepanned — one on one side of the skull, three on both sides — whereafter the dura corresponding to the trepanation orifice was removed. A piece of gelatine film was then inserted on one side, its margin extending under the edge of the cranial defect, whereafter the trephined piece of skull was replaced and the wound closed. In the case of the three animals the other side served as a control: no dura substitute was inserted, but the operation otherwise was exactly the same.

The cats were killed one, two, two and three months after the operation. In the unilaterally operated cat we found that the operation had been favourable, in so far as there were no adherences between bone and brain, whereas the examination of the other three cats revealed broad adherences, which could not be divided without tearing off a small piece of cerebral tissue. On the control sides there was no adherence in one case, in the other two there was less pronounced adherence than on the film side.

Accordingly, the gelatine film we used must be described as unsuitable as a substitute for the dura mater. On attempting to make the film less susceptible to cell invasion and tissue adherence by preparing it with mandelic acid anhydride, potassium dichromate or sodium oxalate the result was a rather rigid and

<sup>1</sup> For kindly preparing the gelatine films and for procuring the polythene films used in the animal experiments, as well as the polythene plates used as bone substitutes on animals and patients, we extend our thanks to the "Ferrosan" Drug Company, Copenhagen.

fragile film which, when inserted sterile intraperitoneally into rats was still found to cause adherence. And as at the same time a publication appeared on the usefulness of polythene film as a substitute for the dura mater, we proceeded to test the latter product.

### Experiments with Polythene Films and Plates.

Polyethylene is one of the modern plastics. It is made under high pressure as a polymerisation product of ethylene and has come into wide practical use, for example in the cable industry, for tubing and for containers, and, in the form of film, as packing material (AISTRUP).

In medicine, polythene has been used by GUENTHER, GRINDLAY & LUNDY and by BROWN, GRINDLAY & CRAIG, who employed it for manufacturing capillary-size tubing for continuous venous infusion and as a dura-mater substitute, for which they employed films that had first been implanted in experimental animals: dogs and monkeys, subsequently in patients. They found that polythene film is an excellent substitute for the dura: it can be sterilized by boiling or with chemicals, holds a suture, is non-absorbable and causes no tissue reaction. They also found that with polyethylene tubing it was possible to form permanent fistules between the lateral ventricles and the subarachnoid space. In the same manner polythene tubing was employed as anastomotic tubing in the bile ducts, trachea and colon.

*Animal experiments.* For our own experiments we used polythene film 0.10 mm. thick and sterilized with formalin, and by means of subcutaneous, intraperitoneal and intrathoracic application on rats found that it is unabsorbable and induces no tissue reaction, except that in a few instances, in which the film had remained in the animal for three or four weeks, we observed a thin fibrinous membrane around it or on a part of it. Microscopy proved this membrane to be built up of connective tissue with a few round cells and polymorphonuclear leucocytes, and it could be seen both with the naked eye and with microscope that the film lay freely in the membrane.

In one rat a bag of polythene was placed about one kidney, from the surface of which there was slight haemorrhage caused by the manipulation. On being inspected two weeks later it was found that the film had partly slipped off and it was seen that

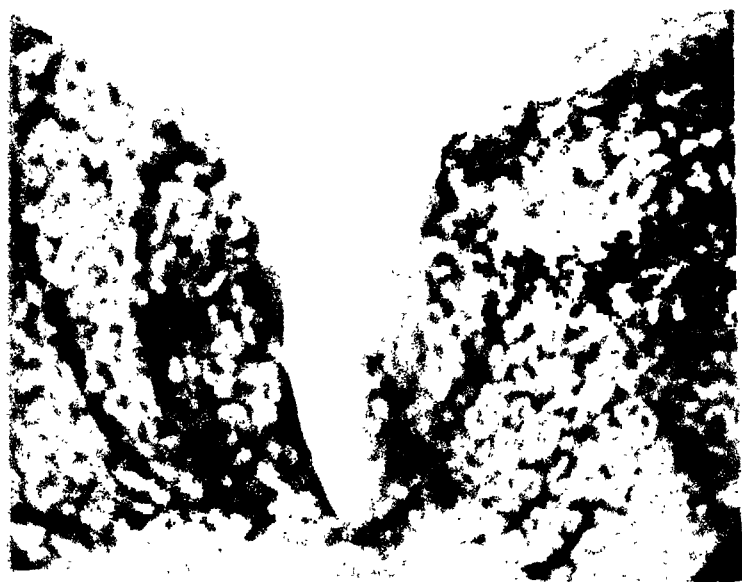




Fig. 3. RH NK 01806. Polythene film as a dural substitute after extirpation of parasagittal meningeoma. The brain is clearly visible through the transparent film, whereby haemostasis can always be verified. The film was sutured to the dura with silk 0.



Fig. 4. RH NK 01855. Polythene plate (0.5 cm. thick) employed for covering a skull defect after excision of cavernoma in the parietal bone. Holes are made in plate and skull with an electric drill for fixing with linen thread.

there were no adherences between kidney and film or between film and surrounding tissues. In another rat a piece of film was placed within an incision in the kidney, gelatine-sponge being applied to both sides of the film as a hæmostatic. After two weeks the film was still in position and it could be seen macroscopically and microscopically that the film had been instrumental in forming a fissure in the kidney (fig. 1). In three rats a defect was cut in the abdominal musculature and covered with polythene film, and a week later it was found that no adherences had formed between film and intestines, whereas the latter were adhering to the abdominal wall which was not covered by film.

The film was also tested on a rabbit, being folded in two layers about a. carotis and drawn forward into the skin wound, the advantage of this being that the same vessel could be employed twice with an interval of over a month: at the second operation the vessel could be brought forward into the wound — freely without adherences — by pulling the film immediately after the incision.

The American experience of the practical usefulness of polythene film as a *substitute for dura mater* was verified by experiments on three dogs operated bilaterally in the same manner as the cats on which gelatine film was tested. In two of the dogs a small defect was also produced in the surface of the brain with the red-hot point of a pair of forceps. The animals were killed 6, 8 and 10 weeks after the operation. In all cases there were adherences between bone and brain on the control side, but in none of the animals were there any adherences between the polythene film and the brain, which in one of the dogs was adhering to a thin membrane which covered but was not adherent to the film. In two cases the polythene film had formed a bulge which left a slight impression on the brain. In all cases dura was adherent to the skull at the site of the operation.

It would seem that polythene has not previously been employed as a *bone substitute*, though BROWN, GRINDLAY & CRAIG say that presumably it may be employed cosmetically for covering the anterior burr holes after transfrontal craniotomy. As there seemed to be a probability that polythene plates would be useful as a bone substitute in cranial defects, two cats were trepanned bilaterally and, in the place of the piece of bone removed we introduced a piece of polythene of similar size but somewhat thicker ( $2\frac{1}{2}$  mm. thick). When the animals were killed about

six weeks later the pieces of polythene were found in place without having accreted to the bone and without adhering to the dura, which in one animal had been left intact, while in the other it had been perforated in the operation. Microscopy showed the polythene disc to be free, but on both sides covered with a thin membrane of connective tissue, as will be seen in fig. 2.

### Clinical Tests.

In clinical neurosurgery it has always been a problem to find a suitable dural substitute when the dura has to be removed, either because of tumour invasion or because of dilaceration owing to trauma. Many tissues have been tried from calf amnion to pig bladder, but so far it would seem that most workers have selected *fresh human fascia*. This is taken from fascia temporalis in the case of small defects and if this fascia is exposed in the wound, and from fascia lata if the defect is large. The particular drawback in this technique is that transplantation of fascia leads to the formation of adhesions between the fascia and the underlying pia mater, adhesions which may be a factor in post-operative epilepsy. It was therefore a great improvement when INGRAHAM & BAILEY 1944 introduced fibrine film for this purpose, as both experimental and clinical tests showed that the film did not give rise to adhesions. Shortly after the end of the war the Department of Neurosurgery of the Rigshospital was sent a supply of "fibrine film" by friends in America and used it with the same good results as INGRAHAM & BAILEY. Later, when *polythene film* was introduced, we also received generous samples of it from Dr. FRANC D. INGRAHAM. The polythene film was 0.06 mm. thick and it is so strong that it is excellent for suturing. We have now used it in 51 cases without ever seeing complications. One great advantage is that even after the dura has been closed it is possible to verify that haemostasis is complete, the film being fully transparent (fig. 3). Its chief advantage, however, is that as the film is biologically inactive, no adhesions are formed to pia or brain. For the rest we have nothing to add to the good results reported by the American workers.

While working with polythene film as a dural substitute we had the idea of trying thicker plates of *polythene to cover skull defects*. In international neurosurgery no agreement has ever been reached as to the best method of covering such defects. Some

employ *tantalum*, whereas others object that it not uncommonly does not heal in, that it is heavy, and that it always makes subsequent X-ray examination difficult because of the massive roentgen shadows cast by the metal. Nevertheless, tantalum was in wide use during the war and several have declared their satisfaction with it. *Acrylic acid prostheses* have been employed for many war wounds, especially in England, but it calls for rather complicated processes involving making casts of the defect, which means several operations. The advantage of prostheses of tantalum and acrylic acid is that they can be moulded to fit the individual case, a matter of particular importance in fronto-orbital defects which not only are cosmetically serious but may also cause disabling headaches and vertigo when the brain glides forward into the defect when the patient bends over.

We have tried tantalum but found it heavy and awkward to work with, an objection also applicable to *stainless steel*; in the end we adopted dead *human bone*. It was treated as follows: The bone is washed thoroughly in ordinary soap and water and then boiled for three hours in distilled water, the water being changed every half hour. The bone is then soaked for twelve hours in 6 % hydrogen peroxide, rinsed in running water for six hours and then dried. It is boiled for 20 minutes in physiological saline before use. After these processes the bone is somewhat soft, is easily shaped to the defect with rongeurs and secured in it with linen thread. Of the 16 cases in which we have employed this technique the transplant failed to heal in smoothly in only one, and this was due to infection; this subsided after local penicillin treatment for six days.

The results from this technique may thus be said to be good, but there are certain aspects that are not ideal. Even in dead bone, processes always occur after transplantation, processes which affect the calcium content of the bone and also give rise to an aseptic inflammatory process, which is never desirable so near the brain. Having had such good results with polythene film as a dural substitute we therefore tried a thicker plate of the same substance for covering skull defects. Polythene for this purpose is obtainable in the form of a greyish opalescent plate, 4 to 6 mm. in thickness, fairly flexible but firm and solid. Before use the plate is boiled for ten minutes, whereafter it can be moulded and fitted to the shape of the defect with strong scissors. The edge is bevelled with a knife or electric cutter to prevent



the plate from sinking inwards and with linen or nylon thread it is secured through holes in plate and the edges of the defect made with an electric drill (fig. 4).

We have now employed this method in 8 cases; and they have all healed in smoothly and formed a good and strong cover. The advantages of this technique are that the transplant is always available, that it can be shaped to the actual defect without difficult or complicated methods, that there are no tissue changes around or in the plate, and finally, that subsequent roentgen examinations are not interfered with.

### Summary.

1. *Gelatine films* prepared in various ways were tested and found unsuitable as a dural substitute.

2. Animal experiments confirmed that *polythene film* is unabsorbable and that after subcutaneous, intraperitoneal, intrathoracic and other applications it causes little or no tissue reaction. When used as a dural substitute on animals and a large number of patients the authors had the same good results as those obtained earlier by American workers.

3. It was demonstrated by animal experiments and by clinical tests that *polythene plates* are a most excellent bone substitute in skull defects, being easy to procure and to mould, causing no tissue changes and not interfering with subsequent roentgen examination.

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## On Sacrococcygeal Teratomata.

By

M. SULAMAA and E. K. AHVENAINEN.

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Teratomata are typical tumours of children. The literature dealing with them is not extensive, in particular with regard to clinical data the publications are based on a few cases only. Nor have the results of treatment been satisfactory. The pathological anatomy of teratoma has been examined more extensively, but the opinions as to their nature are still contradictory. The rarity is perhaps partly apparent, since at the Surgical Department of the Children's Clinic in Helsinki (chief: M. SULAMAA, M. D.) 8 cases were found within a little more than 1 year. The results of treatment having been very encouraging and the histological examinations of the cases apt to throw some light on researches concerning these tumours, we have deemed it advisable to make a report on these cases.

*Case 1* was a girl aged 9 years. The main part of the teratoma was formed by a cyst with one cavity. At the age of 3 years it had produced symptoms of intestinal stenosis and later got infected from the rectum, which led to an incision. Severe recurring suppuration persisting from the fistulae, she was subjected at the age of 7 years to anus praeter sigmoideus and the case then left to itself. An X-ray-examination at the Children's Clinic brought to light that the fistulae had no connection with the rectum. The evacuation of the tumour caused no difficulties, although the anterior wall of the tumour was firmly adherent to the rectum. Later, on closing up of the sigmoidostomy, the patient was able to evacuate her bowels in the usual way and was removed from the hospital as cured. In the thickwalled cyst of the tumour there was a hard part in the wall of the size of a plum, and inside it gelatinous compartments of different size. Patho-anatomic examination (see table No. 1).

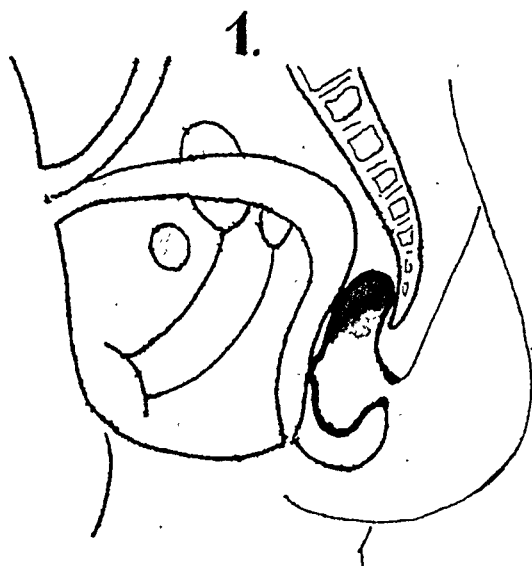


Fig. 1. Case 1.

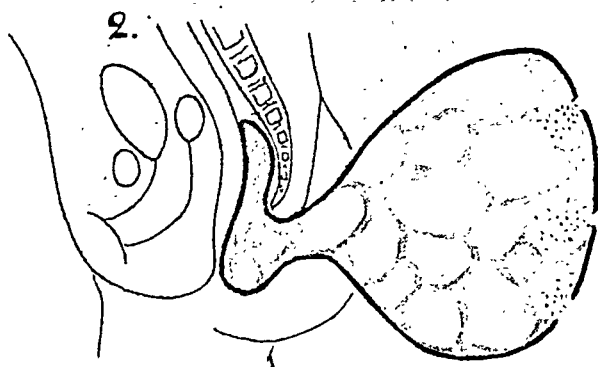


Fig. 2. Case 2.



Fig. 3. Case 2 before operation.



Fig. 4. Case 2 after operation.

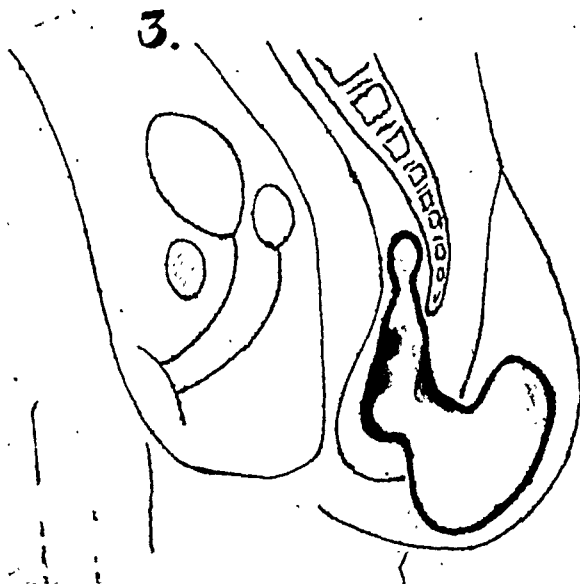


Fig. 5. Case 3.



Fig. 6. Case 3 before operation.

*Case 2* was a girl 14 days old. In the process of labour the superficial cysts of the teratoma situated on the buttocks had burst. At the maternity hospital the tumour was misdiagnosed as myelocoele. In spite of the suppuration of the superficial cysts the tumour was radically removed. Due to infection the wound partly healed per secundam, but recovery was uneventful. The tumour was of a head's size, the tissue was clearly defined from its surroundings, its consistency evenly soft. Inside there were numerous cysts of different size, containing gelatinous fluid. The surface cysts were filled with pus.

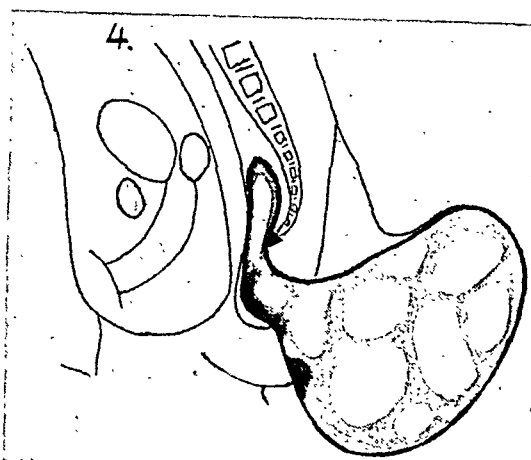


Fig. 7. Case 4.



Fig. 8. Case 4 before operation.

*Case 3* was a teratoma cyst with two compartments in a girl aged 7 months, mainly situated between rectum and sacrum. The radical evacuation was a success, although the contact with the rectum, as also in the other cases, was close. Recovery was uneventful. In the walls of the tumour cysts there was firmer tissue in places. Contents a mucous fluid.

*Case 4* was a fullterm newborn girl, who had a large flabby tumour hanging in the immediate vicinity of the anus. The operation was carried out on the fourth day of life, and the tumour, which was slightly adhering to the rectum, was completely and successfully removed. The recovery was uneventful. The tumour the size of 2 fists was formed by sections the size of an egg. On the section surface there were several gelatinous vesicles of varying sizes and here and there a firmer tumour substance.

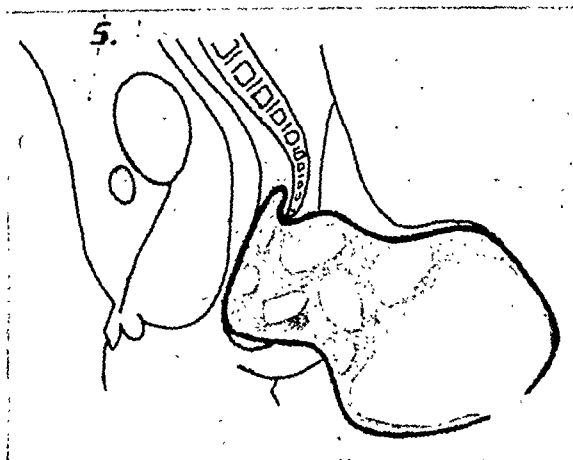


Fig. 9. Case 5.



Fig. 10. Case 5 before operation.

*Case 5* was a premature boy weighing 2300 g. A cystic tumour the size of a fist hanging by its side behind the anus had been torn during labour and ligatured. On the second day of life the tumour was radically removed. Recovery was uneventful until the infant contracted a nosocomial enteritis infection three weeks later and died. The tumour was almost the same large cyst throughout. In the walls of this cyst there were small separate compartments and layers of firm tissue.

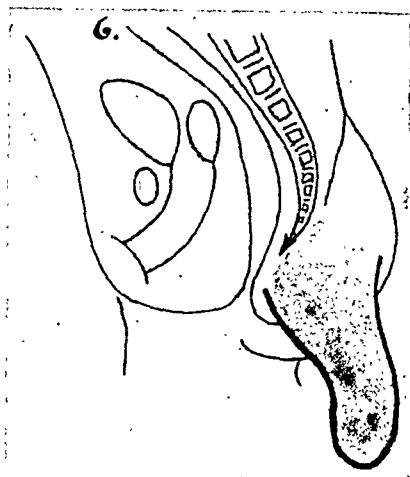


Fig. 11. Case 6.

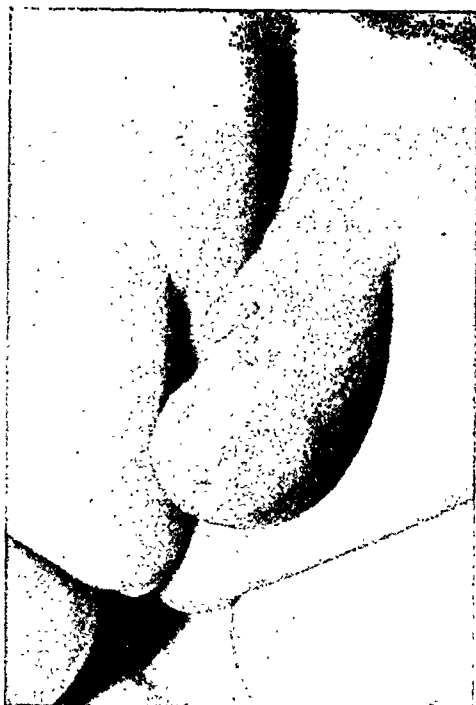


Fig. 12. Case 6 before operation.

*Case 6* was a girl aged 1.5 years who from birth had had a "tail-like" addition in the crena ani on the right side. The X-ray photograph revealed the tumour with a calcificated centre under the os coccygis. During operation the borderline between the surrounding substances and the tumour was not as clearly defined as in the other cases. Owing

to skin shortage the sutures did not hold together but the wound healed per secundam. Recovery was otherwise uneventful. The structure of the tumour covered with normal skin was firm in the surface parts, in the middle spongy, loose. At the proximal end there was a cartilaginous centre.

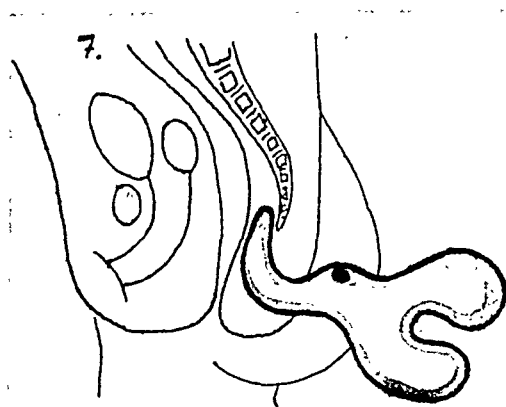


Fig. 13. Case 7.

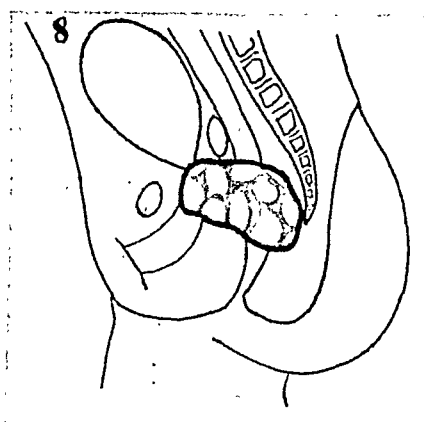


Fig. 14. Case 8.

*Case 7* was a girl aged 1 month who had in the crena ani on the os coccygis a pedunculated tumour resembling a collapsed rubberball. On the surface there was purple, seemingly normal skin. The thickwalled tumourous cyst which had its continuation under the sacrum was easily removed by operation and recovery was uneventful.

*Case 8* was a girl, aged 2.5 months who came to the Children's Clinic because of retention of urine which had begun a month earlier. The development until the seventh week had been completely normal. The bladder could be palpated up to the navel and evacuation only took place by ischuria paradoxa-dropping. The advanced uraemia could not be cured in spite of catheter and energetic fluid balance treatment.



Table  
*Teratomata Substance According*

No.	Bone	Cartilage	Connective Tissue	Muscle	Fat	Cavities			
						Form of Epithelium			
						High-prism.	Iso-prism.	Low-prism.	Flat-tened
1	+	+	+	+	+	<sup>1</sup> +	—	+	+
2	—	—	<sup>3</sup> +	—	—	—	<sup>4</sup> +	—	—
3	—	+	+	++	+	+	—	—	<sup>5</sup> +
4	—	+	+	+	+	+	—	+	<sup>6</sup> +
5	—	+	+	+	+	+	—	—	<sup>7</sup> +
6	+	+	+	+	+	—	—	—	—
7	—	—	+	+	+	+	—	<sup>8</sup> +	—
8	—	—	+	+	+	+	—	<sup>9</sup> +	—

<sup>1</sup> Epithelium resembling intestine.

<sup>2</sup> Mucous (salivary) gland.

<sup>3</sup> Only in the middle of the nerve tissue around blood vessels.

<sup>4</sup> In the middle of the nerve tissue there are also cavities without epithelium.

<sup>5</sup> The height of the epithelium varies even in the walls of the same cavity. Cavities without epithelium are found in the muscular tissue.

Death occurred already in two days. The autopsy revealed as the main cause of death a subdural haemorrhage in the parietal region which was considered to have developed on the basis of uraemia. In the minor pelvis encircling the rectum and the neck of the enlarged bladder a teratoma with several cavities, was found, formed chiefly by cysts with thin walls. Both kidneys were hydronephrotic.

### The Pathological Anatomy of the Teratomata.

For microscopic examination several specimens were taken from different parts of the tumours. The paraffin sections were dyed with Wiegert's haematoxylin and van Gieson as well as with Delafield's haematoxylin and eosin. The frozen sections taken from corresponding places were dyed with Delafield's haematoxylin and Scharlach-R. Of the cases No. 2, 7 and 8 only 4—5 paraffin sections of each were available. The tissue elements found in the microscopic examination are presented in table No. 1.

The classification of the teratomata was very complicated in earlier literature. MERKEL, H. classifies "I. Mischgeschwülste,

## No. 1.

## to Microscopic Examination.

Contents	Glan- dular Tissue	Central Nervous System	Lymphoid or Blood Vessel Tissue.
Mucous	<sup>2</sup> ++	Glia, some ganglion cells.	Lymphatic, "lym- phatic gland"
Inflammatory cells. Seromucous.	—	Glia and membranes	++
Mucous	—	Choroid plexus in the wall of the cavity.	++
Seromucous	+	Glia	Hemangioma type
Serous	+	Choroid plexus in the wall of the cavity.	Hemangioma type
—	+	Ganglions	Hemangioma type
—	+	Glia and nervous fibres.	+
Squamae, sebum and serous.	<sup>10</sup> +	Differentiated C. N. tissue.	+

<sup>6</sup> Cornified skin epithelium with lanugo hairs.

<sup>7</sup> In places papillae covered with high-prismatic epithelium in the walls of the cavities.

<sup>8</sup> In some places resembling intestinal epithelium, in others skin epithelium.

<sup>9</sup> Skin epithelium which is cornified and contains hairs and sebaceous glands.

<sup>10</sup> Sebaceous glands in the skin and besides pancreas-like tissue.

a) mesodermale, b) mesoentodermale, bzw. mesoectodermale. II. Die komplizierten Dermoide, Teratome und Teratoide." — At the close of the last century BORST, J., ENGELMANN, H. and LINSER, P. debated whether the appearance of sacral teratomata is to be interpreted as a bigerminal *i. e.* foetal inclusion or as monogerminal *i. e.* foetal medullar remains and disorders of the development as well as an overgrowth. HARTENSTEIN, H. J., HEIDENHAIN, L. & GRUBER, G. B. and SCHRAMM, H. are of the opinion that the sacral tumours are malformations of different primitive germ layers but nowadays they are generally considered to be true tumours. Thus EWING, J. says: "The recent tendency has been to regard the congenital mixed tumours of the sacral region as forms of true teratomata, a view which is favoured by many considerations." WILLIS, R. A., who thoroughly investigated the microscopic structure of teratomata is of the opinion that "A teratoma is a true tumour or neoplasma composed of multiple tissues of

kinds foreign to the part in which it arises". According to the investigations of WILLIS, R. A. all teratomata are tridermal and in  $\frac{3}{4}$  of them nerve tissue can be demonstrated.

Our cases as well speak for the tridermal character of teratomata (see table No. 1). More or less differentiated substances of nerve tissue were found in all our cases. The structure resembled that of tumours and no "complete" organs could be ascertained. The notion of WILLIS, R. A. that "teratomas are tumours arising from foci of plastic pluripotential embryonic tissue escaped from the influence of the primary organizer during early embryonic development" is thus supported by our cases.

No histological signs of malignity were found in our cases. Nor have relapses or metastases been ascertained so far during clinical observation of these cases. As a matter of fact, benignity has generally been ascertained, although carcinomatous degeneration has been found even during childhood. (PANDALAI, K. G., STEWART, J. D., ALTER, N. M. GRAIG, J. D., and LISCO, H.).

Of the material of WILLIS, R. A. containing 82 teratomata only two were localised to the sacral region. According to WILLIS the most usual localisation is to the ovaries, after that to the testis, the retroperitoneal region, the mediastinum anterior and, lastly the sacrococcygeal region together with the basis of the skull. According to MAC CALLUM, W. C. the sacrococcygeal region is the most common seat of teratomata.

According to our opinion the sacrococcygeal region is by far the most common in babies, since during the same period — 1 year and a half — in which these 8 cases accumulated, not a single case with localisation to another region was ascertained in our clinic.<sup>1</sup> Of course, in the other localisations mentioned above, tumours free from symptoms are more apt to be overlooked in infants than the easily perceptible sacral tumours. On the other hand, however, at least the testis tumours would more often be observed among our extensive material if their incidence were greater than that of the sacral teratomata. The greater predisposition of the female sex to teratomata is generally known, and it is also supported by our ratio 7 : 1.

<sup>1</sup> During the time of printing 2 more cases of sacrococcygeal teratoma (resembling most cases 4 and 5) were later treated successfully, while there were other localisations of 2 ovarian and 1 thyroid teratoma. One case of rectal duplication caused difficulties in the differential diagnosis. It was found at the time of operation that its wall was thicker than that of teratoma, its inner surface resembling mucous membrane also macroscopically, and its adhesion to the rectum was close (organic).

## The Clinical Significance and Treatment of Sacrococcygeal Teratomata.

The sacral teratomata, being generally benign as explained above, do not have any particular significance, unless the pressure symptoms caused by them on one hand and infection on the other create a danger to life. Case 8 of our material is a typical example of the pressure symptoms and in case 1 these also appear to a lesser degree. It is probable that in case 8 a considerable discharge of fluid into the cysts of the tumour did not take place until the 7th week, when the symptoms set in. Why this happened is unknown. There is a history of diarrhea symptoms in the first instance, after that difficulties in urinating, so that an increase of fluid due to inflammation can be presumed to be the reason of the sudden growth. WOODRUFF, S. R. and BEGNER, J. A. describe a similar case of urine retention in a 5 months infant with a fatal course. The thinwalled cysts of large tumours easily become torn and infected during labour as in cases 2 and 5, or they are infected later, for instance through the rectum as in case 1. On the other hand, complications appearing in tumour cavities due to infection can be persistent and institute a danger to life.

With regard to the prognosis of operation the teratoma literature presents a fairly discouraging picture. Our own experiences of the chances of operation are positive throughout, with the exception of case 8, brought in too late. Considering that in these operations it is a question of a clearly defined, easily extirpated tumour, which usually is situated in an easily accessible region, the difficulties and causes of failure are the same as in infant surgery in general. It is first and foremost a question of deciding on the optimal moment for the extirpation. The evacuation of small and harmless tumours can with good reason be postponed to the second year of life, since the general mortality in infant surgery falls rapidly after the nursing age is left behind. We are of the opinion that the infrequency of malignity justifies such a postponement, if the child's general condition is poor. On the other hand, cases which have been ruptured during labour, or such which present easily infected cysts, especially very large teratomata, must preferably be operated upon immediately after birth, when the anus is not yet so infectious as later. The surgical wounds

are preserved from contamination by excrements and urine in open treatment under a heated cradle. Where the most usual types of tumours are concerned, such as the cases 1—7 in our material, there are no technical difficulties worth mentioning, since the excision of the tumour can generally be performed without damaging the rectum. The removal of such tumours which are situated deeply in the pelvis, as for instance case 8 or at least the temporary evacuation of the tumour cysts by puncture must be attempted immediately on the appearance of the pressure symptoms, before incurable damage has been caused. Since the removal can be technically a very exacting measure in such cases, a postponement is justified, provided it does not endanger the prognosis.

### Summary.

The authors describe 8 sacrococcygeal teratomata, 7 of which were operated upon successfully, but one case with a teratoma crowded into the pelvis, was brought in too late for treatment and the result was death from uraemia. Neither patho-anatomically nor clinically could any signs of malignity be discovered in any of these cases. The examination speaks on behalf of a true tumour character and a tridermal origin. One "tail-like" formation with a higher histological degree of development than the other tumours was considered as a transition to a malformation. Since 8 cases were ascertained within a year and a half, there being practically no teratomata localised to other than the sacral region during this period, the authors consider this localisation to be the most common one. The clinical significance lies in the rupture of the cysts of the tumour and in infection, as well as in the compression of the organs in the pelvis. These complications require immediate treatment, while in the opinion of the authors the removal of the harmless tumours can be postponed until later, if the infant's general condition is not good, malignancy being relatively rare. An operation immediately after birth is more favourable than at any other moment during the first year of life due to danger of infection through the anus. The operation is usually a technically easy one.

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## Post-thrombotic Varices.

Results of Phlebography and Radical Operative Treatment.

By

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Varicose veins in a leg that has earlier been the seat of deep venous thrombosis are, as is known, traditionally regarded as compensatory formations, *i. e.* sinuses that have taken over the function of the destroyed deep venous tracks. As regards therapy this view has consequentially led to the opinion that in such cases varices are not to be treated at all or possibly only very cautiously if risk of exacerbating the patient's condition is to be avoided. Radical treatment has quite naturally been considered as entirely excluded.

The results of the work submitted here are of a nature to alter the prevailing view, not least of all respecting the possibilities of treating these cases.

The method introduced by DOS SANTOS of injecting opaque medium into the vascular system to enable the vessels to be actinographed has increased our resources for studying questions belonging to this field. Phlebographical methods have attained very wide application in Sweden of recent years in association with the lively interest aroused in questions of thrombosis and embolism. The methods have been developed more especially by BAUER, LINDBLOM and LÖFSTEDT.

BAUER originally employed phlebography to diagnose an existing state of thrombosis and to localize the thrombus. Later on, however, he considered that he had also shown by phlebography





permanent obliteration of those veins which have been the seat of a deep thrombosis. This view is based entirely on a method of examination that is often misleading.

It is known, of course, that a vein may be definitively destroyed by a deep thrombosis, but it is *a priori* highly improbable that this would take place without exception. The fact is that in such a case superficial and deep veins in the lower limbs would *inter se* react to the thrombotization in opposite ways. Superficial varicose veins that have been obliterated either through thrombophlebitis or through injection treatment are rather frequently seen to be reconstructed by recanalization or sometimes by the establishment of lateral branches. It does not appear very probable that deep veins should behave differently in this respect.

That deep-seated venous thrombi are recanalized is also known from the patho-anatomical literature, in which detailed descriptions may be found of the typical appearance of the recanalized thrombus (BRASS). In transverse section it has the form of a wheel with nave and spokes.

In the majority of leg-ulcer cases examined as well as in cases of thrombosis BAUER found that the deep veins could not be filled. From this he drew the conclusion that to a large extent ulcers of the leg are the result of undergone thromboses even in cases where so far as is known the patient has not had any thrombosis. The term "ulcus varicosum" ought to be replaced by "ulcus post-thromboticum". However, the fact that the method of examination has not been free from objections leaves the assumption unproven.

At the Surgical Clinic of the Maria Sjukhus and, after this hospital was disestablished, at the Surgical Department II of Södersjukhuset a very large material of varices has presented itself during the present decade.

This material naturally includes not so few cases of post-thrombotic varices. On the initiative of the chief of the Department — Dr R. BRANDBERG — these have been submitted to an ever-increasing extent to phlebography in order to ascertain the conditions of the deep veins.

It is the purpose of this paper to submit a report of the results of these examinations and of the radical interventions thereafter undertaken against the varicose veins.

Varicose veins are treated here on the same principles as are at present common at the Swedish hospitals. Processes that are but little spread receive only injection treatment. Disseminated varices always have a valvular incompetence of the saphenous vein and are operatively treated. Recourse to operation is also had in limited processes if the saphenous vein is incompetent, as otherwise the danger of recurrence is great.

At operation the saphenous vein is ligated and divided at the fossa ovalis, whereupon the upper portion of the vein is extirpated by BABCOCK's method and *etolein* is then injected in a distal direction from the lower point of division. If there are communications further down between the saphenous vein and the deep vessels, the vein is also divided at the popliteal space and in these cases the sclerosing injection is made from this point.

We lay great stress on the extirpation of the upper part of the saphenous vein. At least 15 centimetres, preferably substantially more, ought to be removed. By this means the development of collateral tracks is rendered more difficult as is also a recurrence of the condition.

Obviously there will often be a number of varicose loops that are not thromboticized by the single injection made at the operation. In such cases the treatment is supplemented later or by some percutaneous injections of *etolein*.

Since this investigation was started more than four years ago, first of all at the X-ray Department of Maria Sjukhus, then at the Radio-Diagnostic Department II (Chief: W. MAGNUSSON) of Södersjukhuset, one or both legs of 257 patients have been phlebographed. Most of the patients were remitted for examination from the Surgical Department II. A small number came from the Surgical Department of Ersta Sjukhus (Chief T. SILFVERSTOLPE) and were kindly placed by that Department at our disposal for after-examination, etc.

The cases consist of post-thrombotic varicosities as well as varicose cases with an unclear history in which on account of swelling, large leg ulcers and other pronounced changes it was considered not improbable that a post-thrombotic state was concerned. A number of cases of simple varices were also examined in order to have a normal material for guidance in the appraisal. Included in the above figures are also a number of cases with fresh thrombosis on which phlebography had been carried

out to confirm the diagnosis. These last two groups comprise 44 patients, which are not included in the subsequent account.

Of the remaining 213 patients, both legs were examined in 39 cases, and hence the material considered below consists of 252 phlebographed legs.

We have mainly directed our attention to the cases having a history of deep-seated venous thrombosis. As such, only cases have been taken in which a physician had made the diagnosis and considered it indicated the prescription of treatment directed against thrombosis, usually prolonged rest.

For cases attended in hospital the diagnosis has been largely verified by reference to the hospital journals. For those attended at home or for those concerning which information could not be found in the records of the hospitals the diagnosis has not been considered as certain until after detailed information has been received concerning the physician's instructions to the patient as to symptoms, decumbiture, etc.

In all these cases, therefore, it is considered as established that deep-seated venous thrombosis has actually been involved and not merely superficial thrombophlebitis, which is often given the same name in common Swedish parlance.

Of the 252 phlebographed legs it has thus been regarded as confirmed in the case of 155 that they had earlier undergone one or more deep venous thromboses, and in 113 of these free deep venous tracks have been roentgenologically demonstrated.

Hence in 73 % of the cases that had undergone venous thrombosis free deep venous trunks have been found on phlebography.

The thromboses date back from 33 years down to 1 year, the mean time being 11 years. Hence, most of the cases originate from the period when prolonged bed rest was the recognized method of treatment for deep thrombosis. Only in very few cases had recourse been had to modern treatment with heparin or dicoumarin and early rising.

The post-thrombotic material of varices is distributed as follows (see table 1, page 435).

After having established the presence of free deep venous tracks by X-rays we have considered ourselves at liberty to recommend the patients to have their varices operated upon, and of the 113 recanalized thrombotic legs 54 have hitherto undergone operation.

Table 1.

*Distribution of the Post-thrombotic Phlebograms.*

		Deep Venous Tracks free	Tracks not free	Total
Males,	Number .....	23	16	39
	Right Leg .....	11	5	16
	Left Leg .....	12	11	23
Females,	Number .....	90	26	116
	Right Leg .....	26	8	34
	Left Leg .....	64	18	82
Males +	Number .....	113	42	155
Females,	Right Leg .....	37	13	50
	Left Leg .....	76	29	105

Right/left distribution =  $\frac{1}{2}$   
Male/female distribution =  $\frac{1}{3}$

These 54 consist of 11 males and 43 females. One male and one female have been operated bilaterally, and hence 52 patients are concerned.

At follow-up examinations of those operatively treated it has been possible to obtain data on 42 of the legs. Some patients could not be traced, other were not examined because the date of the operation was less than three months back in time. Many presented themselves at the hospital for examination, others answered by letter or telephone.

The operative results are distributed as shown in the following table.

Table 2.

*Follow-up Findings.*

	Males	Females	Total
1) Subjectively free from trouble	6	17	23
Varices healed			
Leg ulcers (if any) healed			
2) Subjectively essentially better	2	14	16
Leg ulcers (if any) healed			
Have varices left			
Swelling improved			
3) Unimproved .....	2	1	3

One patient was in a worse condition but the operation was found to have been based on an erroneous diagnosis. Re-examina-

tion of the roentgenograms revealed an overlooked obstruction several centimetres long in the popliteal vein.

Three patients were unimproved, their varices having recurred a short time after the operation. It is a remarkable fact that in these cases the operating surgeon had not adopted the procedure earlier described as our normal method. He had contented himself with ligating the saphenous vein without extirpating its upper portion. These cases seem to confirm the accuracy of the value we attach to this extirpation.

The rest of the patients were entirely free from trouble or essentially improved. Among the latter were a series of patients who had some small varicosities left and who, at the follow-up, were therefore recommended supplemental injection treatment. Immediately after the operation they had evidently felt so free from their affection that they had not considered it necessary to return for the recommended injection treatment.

A close questioning of the patients who stated that they were entirely free from trouble in the operatively treated thrombotic leg brought out the fact that most of them nevertheless felt a certain difference between this leg and the healthy one. The aching pain in the leg had vanished, but following exertions a feeling of heaviness may arise that can be moderately troublesome and further, after rather considerable strain, it sometimes occurs that the leg swells below.

The explanation must be deemed to be that the recanalized veins are not functionally fully competent in spite of the radiogram having shown no anatomical defect. The vein wall may be stiffer than normally and have difficulty in adapting itself to a rapid blood flow, valvular injuries may be at work, and still other explanations are perhaps conceivable.

That thrombosed legs have become well or at least highly improved from a successful varicose vein operation is of great interest. Firstly, it affords an elegant confirmation of the X-ray demonstration of functioning venous channels, secondly, it supplies a new conception of the character of varices after thrombosis.

At the outset the varices of these patients must have constituted vicariously acting blood channels, but after recanalization had been effected they lost their character of necessary collateral tracks and became established solely as varices. As such they had given

rise to the main part of the leg trouble experienced by the patients. Hence, these patients had suffered from varicose vein disease and not, as one is accustomed to view the matter, from an affection depending on reduced circulation in the deep blood-sinuses.

In the material presented here free deep venous channels have accordingly been demonstrated by X-ray examination in 73 % of 155 cases which had earlier had deep venous thrombosis. This high figure, however, is doubtless only to be regarded as a minimum one, for, as previously stated, it must be borne in mind that in spite of the progress of phlebographical technique the failure of the opaque medium to fill the vein does not prove the latter to be obliterated.

The material submitted contains a case which confirms that no binding conclusions can be drawn from the fact that the deep veins are not filled with dye at phlebography. In this patient these tracks were not filled in the thigh and it was considered that the saphenous vein could not be ligated higher up than the popliteal space. The operation resulted in an immediate improvement of the patients' affection. One month after the operation she fell ill, however, with an acute thrombophlebitis extending from the knee up to the fossa ovalis. After this had healed in a short time the patient became practically entirely free from her leg symptoms. The deep channels must in this case have been patent in spite of their non-visualization on the roentgenograms.

### Summary.

155 legs which had earlier been the seat of deep venous thrombosis have been examined by means of an improved phlebographical technique.

Of these, 73 % (113 legs) have presented free venous channels at the examination, the thrombosed veins having accordingly been recanalized.

It is pointed out that 73 % is a minimum figure.

Among those found to have free deep venous channels 54 have been operated upon radically for their varices, and the majority of these have admitted of being followed up. They were found to have become entirely well or to have improved to a high degree, with the exception of three cases which had undergone early relapse owing to a less appropriate operative procedure.

In deep venous thrombosis varices initially play an important part as compensatory blood-sinuses, but in the majority of cases where recanalization of the deep veins is effected this function ceases and the varices remain as a purely pathologic change. After radical treatment of the varices these patients become free from symptoms or very much improved.

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## Fractures of the Upper End of Humerus with Great Displacement Treated by Marrow Nailing.

By

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med. lic.

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The treatment of fractures at the upper end of the humerus seldom presents great difficulty. It is sufficient for most of these fractures to support the arm in a sling for some weeks and begin early with active motion. The functional result will be good even if the fracture reposition is not entirely exact.

However, there is a small group of this type of fracture where the displacement is considerable and reduction seems necessary. The commonest method is closed reduction, possibly combined with an abduction frame with or without traction. Satisfactory positions are usually obtained with this technique but the reduction is sometimes technically difficult and it can also be troublesome to maintain the position. The use of the abduction frame is also rather trying for the patient.

It is therefore not surprising that some surgeons favour open reduction. To fix the fragments different means have been used: intramedullary ivory peg (ZIELKE), Kirschner wire (BRATTSTRÖM) and Smith-Petersen nail (DEBEYRE and RENÉ). Closed reduction and fixation with the Küntscher nail has been described by SCHMUTZLER.

During the last four years we have used open reduction and fixation with the Küntscher nail in 21 cases. The total number of fractures of the surgical neck of humerus treated during the same period was 264. This shows that operation was found necessary in a relatively small percentage of the cases.



## Operative Technique.

The humerus is uncovered by a short incision over the deltoid tuberosity. An oblique canal is chiseled through the cortex and a Küntscher nail of the appropriate size is driven in so that the point of the nail lies exactly distal to the fracture. The fracture is then uncovered by another short incision over the forward part of the deltoid muscle. The muscle fibres are split and the fracture is reduced. The course of the long biceps tendon is noted. If the tendon is angled, this indicates that the fragments of the bone are rotated. When the reduction is completed, the nail is driven into the proximal fragment. Usually a good fixation is obtained.

The patient remains in bed for a few days after the operation with the upper arm suspended in a vertical position. Thereafter he may be ambulatory with the arm supported by a sling. The fracture is stable after the operation and active motion, which is begun immediately, may be carried out without pain. The stay in hospital is usually from two to three weeks.

When bony union was established the question of removal of the nail was considered. However many of the patients had recovered function so well that they would not willingly submit to further operation. Only in five cases has the nail been removed. In those in which it has been left no untoward results have occurred. If marrow nailing is carried out on a child, the nail should always be removed when the fracture is united.

## Complications.

In one case, two complications occurred:

Case K. J. Male, 47 years old. Injured by a motor accident Nov. 1946 and operated 7 days after the accident. During the insertion of the nail the bone was cracked so that an oblique fracture of the diaphysis resulted. The nail was removed, the original fracture uncovered and reset. The nail was then driven in from the tuberculum area fixing both the new and the old fracture. A good position and fixation was obtained. The fragments united but the mobility was poor. X-ray some months later showed myositis ossificans near the shoulder joint.

The import of this case is that the canal in the cortex should be chiseled sufficiently oblique and wide enough so as to prevent the nail cracking the bone.

No other complications have occurred.



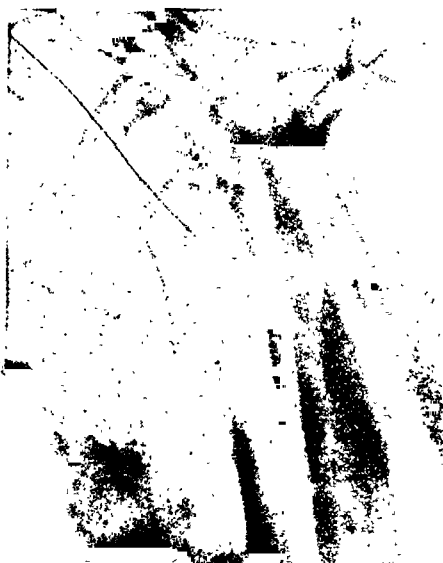
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C



D

Fig. 1 Case A. W. Female, 74 years old.

A and B: Position before operation. Fracture with a backward angulation to about 70°.

C and D: Reduced and nailed in good position.  
At follow-up full movement and no pain.

WIDÉN: Fractures of the Upper End of Humerus.



A



B

Fig 2. Case L. N. Male, 16 years old. Attempts at reduction by abduction frame with traction were unsuccessful. Reduced and nailed in good position. Patient resumed work one month after operation.

A: Before operation.

B: X-ray at follow-up four years later. Full movement and no pain.



A



B

Fig. 3. Case L. K. Child, 5 years old. Several attempts at a closed reduction were unsuccessful.

A: Before operation.

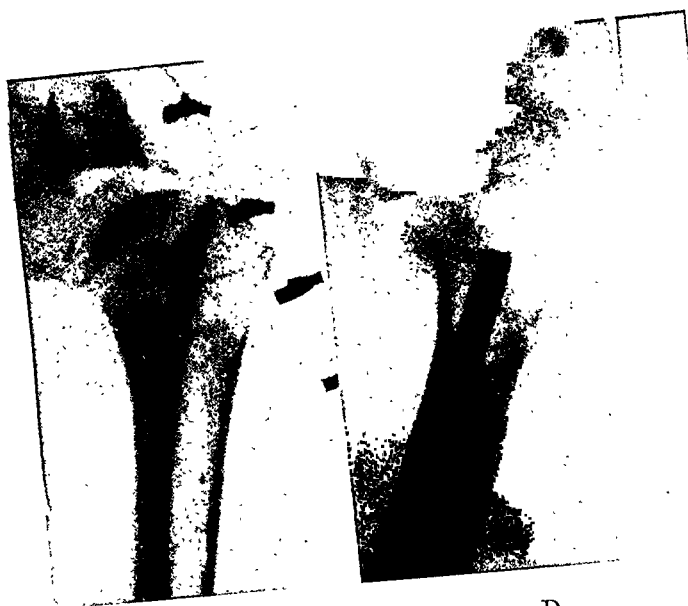
B: Reduced and nailed in good position.

At follow-up full movement and no pain.



A

B



C

D

Fig. 4. Case S. L. Female, 53 years old.

A and B: Before operation. The head is split into three fragments. The central fragment is impacted in the shaft.  
 C and D: After operation.  
 At follow-up, 6 months after operation, the patient could raise her arm 60° over a horizontal plane. She had no pain.

WIDÉN: Fractures of the Upper End of Humerus.



## End Results.

In all, 21 patients have been treated according to the technique described. Two are dead. One died 6 months and the other 2 years after operation. According to information received from relatives, both were fully recovered from the fracture. They were free from pain and had good movements. Contact with one case was lost.

The remaining 18, 13 females and 5 males, have been followed up. The interval between operation and follow-up varied from 6 months to four years.

In 13 cases the result was excellent. These patients were free from pain and either had fully normal movement or less than 10° limitation of complete range of upward movement. The patients considered themselves to have fully recovered.

In 4 cases the result was only fair; all were free from pain and able to work. They could not, however, raise the arm more than 40°, 50°, 60° and 60° respectively, over a horizontal plane. In two cases, the outward rotation was decreased to about half of the normal.

In the one case, complicated by myositis ossificans, the result was poor.

It should be noted that 11 of the patients were over 60 years old at the time of operation. The results with the old patients have proved to be as good as the young.

## Summary.

1. In fractures at the upper end of the humerus with pronounced displacement good results have been obtained by open reduction and fixation with the Küntscher nail.

2. Compared to treatment using the abduction frame, this method is more convenient and less painful.

3. The method can be used even for elderly patients.

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## Disposal of the Bronchial Stump in Lobectomy and Pneumonectomy for Bronchiectasis.

By

ERIK UNONIUS,  
M. D.

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Infection of the mediastinum and pleura, with bronchial fistula abscess around the stump, late haemorrhage, and sepsis was, as long as the tourniquet method was used — with or without separate ligature or suture of vessels and bronchus — an overhanging danger in extirpation of the lung and lobe (BRUNN, SHENSTONE, ROBERTS, T. EDWARDS, GRAHAM, ALEXANDER, CHURCHILL). After the introduction of the technique of dissecting the hilus and disposal of vessels and bronchi separately (CRAFOORD, BLADES, OVERHOLT) the number of cases with bronchial insufficiency was greatly reduced. Assessing the results of lobectomy and pneumonectomy JANES says: "It is apparent that attempts to assess the value of these procedures should be based upon those done by the dissection technique, those done with the tourniquet being regarded as of interest only as a stage in the development of thoracic surgery". Dissection, as such, did not, however, ensure satisfactory results. The way in which the bronchi are closed seems to be of great importance. It may be mentioned as an example that OVERHOLT had 52 bronchial fistulae in 68 surgical operations with dissection + ligature as against 7 bronchial fistulae in 58 surgical operations with dissection + suture of the bronchus. Silk, or catgut, or both, were used for the sutures. BELSEY tried closure of the bronchus with steel sutures. Of 27 surgically treated cases, bronchial fistula was demonstrated by

means of lipiodology in two cases. The patients were, however, clinically free from symptoms.

In his work "On the Technique of Pneumonectomy in Man" (1938) CRAFOORD gives a detailed description of his method of terminating the bronchial treatment with invagination. He has used this method since 1934 in pneumonectomy and in 1938 he also introduced it in lobectomy for bronchiectasis.

### Investigation Series.

This investigation was undertaken for the purpose of studying the value of CRAFOORD's method of treatment for closure of the bronchial stump on cases of infected bronchiectasis, and of finding as far as is possible — the origin of the postoperative infection and its manner of spreading.

With this in view I examined CRAFOORD's series of lobectomy and pneumonectomy operations for bronchiectasis, carried out according to his method, during the period July 1939 to the end of 1946. The series comprises 53 cases: 25 males and 28 females, all severely infected. Age at time of surgical intervention: 7 to 52 years, average age 25 years, similar in both sexes.

The preoperative diagnosis was made after a thorough examination. In the majority of the cases all the lung lobes were surveyed with the aid of lipiodology. Each case was bronchoscoped and secretion samples, taken simultaneously, were examined for tubercle bacilli and inoculated into guinea-pigs. Furthermore, complete clinical, laboratory, and X-ray examinations of the heart and lungs were carried out.

### Preoperative Treatment.

Besides general roborant treatment, blood transfusions were given to improve the patient's general condition. For combating the infection and reducing the sputum to the smallest possible quantity sulphonamides (since 1945 a sulpha compound + penicillin) were administered following resistance tests. Together with autovaccine given over a period of one to two months, an endeavour was made to empty the bronchi of secretion by postural drainage. When the amount of pus in the sputum was particularly great the treatment was supplemented by repeated aspiration through the bronchoscope and local treatment with penicillin.



## Operative and Postoperative Treatment.

In order to facilitate rapid administration of saline, blood, and stimulants an intravenous drip was applied before the operation.

An intratracheal tube was introduced following local anaesthesia of the pharynx and trachea. A bronchial tamponage was gently pocked in the bronchus to the diseased lobe or lung. Intubation anaesthesia with the spiropulsator was used; the anaesthetic was nitrous oxide and ether before cyclopropane was obtainable in Sweden. A slight excess of oxygen gas was administered and the patient's respiration could thus be suppressed and ventilation taken over completely by the anaesthetic apparatus.

The chest was opened according to CRAFOORD's method described in *Acta Chirurgica*, 1938. The structures in the hilus of the part of the lung to be resected were anatomically dissected. After ligation of the vessels, the bronchial tampon was removed and the bronchus gripped with clamp forceps. The bronchus was divided and the outermost ring of cartilage removed for the purpose of obtaining a soft stump, easy to invaginate. The edges were coapted with 3 to 4 interrupted silk sutures, avoiding the mucous membrane. The stump was closed with a continuous catgut suture, and the forceps removed. The corners were invaginated with silk and the mid part of the bronchus with a few interrupted silk sutures. In the more recent operations, if the bronchus was very short, the branches of the bronchi were either dissected and combined into one common lumen, which was closed in the ordinary way, or sutured separately and an invagination suture made in the bronchial stump thus lengthened. The wound in the mediastinum was powdered with a mixture of 30,000 units of penicillin (Ca-salt) + 5 grammes of sulphathiazole and the stumps of bronchi and vessels then buried, separately, into mediastinal tissue; the whole area was then closed with a continuous pleura suture.

The lobes were often joined by bridges of lung parenchyma of varying thicknesses. This occurred in 50 per cent of the cases. Narrow bridges up to the thickness of a finger were furnished with a single ligature, and broad bridges with a continuous catgut suture which in turn was invaginated with an additional continuous catgut or silk suture. The same procedure was used in treatment of the resection border between the lingula and the upper lobe.

Before the chest was closed the remaining lung was inflated to normal size and drainage applied — in all but 9 cases — for the purpose of checking pleural exudate and intrapleural pressure. In recent years, drainage has not been used in those cases in which there were no bridges to divide. In uncomplicated cases the drain was removed on the 4th to 14th day.

Pneumonectomy was carried out in 8 cases, ectomy of two lobes (the lingula is counted as a lobe) in 10 cases, and ectomy of one lobe in the remaining 35 cases.

Sulphonamides and penicillin were administered postoperatively, and during the first days oxygen was given through a nasal catheter. If large quantities of mucus hampered the respiration, aspiration was carried out through a bronchoscope or a catheter introduced into the trachea. Saline and blood were given intravenously. The intrapleural pressure was kept under observation, X-ray surveys were made daily during the first days and later at intervals of a few days.

### Results and Complications.

Forty-nine out of 53 surgically treated cases recovered (= 92.4 per cent). *No cases of insufficiency of the bronchial stump occurred, the stump healing in every case by first intention.*

In two cases the wound in the chest wall was infected, in one of them in connection with pleural empyema. The infection was of no importance in the course of healing (Cases Nos. 18 and 23).

In 9 cases (Nos. 5, 6, 12, 22, 29, 41, 48, 52) bacterias were cultivated on one occasion from the pleural fluid, which was perfectly clear. No further findings of bacteria were made. The time of convalescence was the usual.

*Empyema* occurred in 6 cases (Nos. 1, 7, 8, 18, 28, 39). In all but two (Nos. 8 and 28) the infection originated from peripheral divided lung tissue. In Case 8 the cause was probably a primarily infected pleura and in Case 28 direct infection during the operation.

*Case 8.* K. I. 1881/39. Male, aged 19, with bronchiectasis in the middle and lower lobe on the right side. Cough and sputum for 10 years. Purulent sputum for one year. Right-sided empyema healed six months previously. 30. 11. 1939: Lobectomy med. et inf. dx. (CRAFOORD).

Hard, fibrous mediastinal tissue rendered dissection difficult. The lobes were firmly joined together and to the chest wall, with thick, hard rinds. Suction drainage + extrapleural drainage facing the mediastinum under the pleura suture.

Postoperative temperature consistently above 39° C. On 5th day increasing pleural exudate containing streptococci. On 11th day, puncture for pericarditis, and six days later streptococci were found in the fluid. Pleura and pericardium were drained.

Death a little less than one month after the operation, with all the signs of heart failure. Post mortem revealed a well-healed bronchial stump.

*Case 28.* K. I. 103/43. Male, aged 23, with bronchiectasis in entire left lung. From childhood, cough with sputum and for a year large amounts of purulent sputum and several haemoptyses. 20. 4. 1943: Pneumonectomy sin. (CRAFOORD). During the operation a cavity containing pus and staphylococci was encountered.

One week after the intervention suppuration from the drain increased and staphylococci were found. A fortnight later the same kind of bacteria was cultivated from the pericardial fluid. Pleura and pericardium drained. A little over a month after the operation death occurred.

At post mortem a bronchial stump which had healed by first intention was found. There was left-sided empyema and pericarditis, both well-drained, right-sided empyema which had not been diagnosed, and acute oedema in the right lung.

In cases 1, 7, 18, and 39 communication with peripheral bronchi was observed. In all these cases the empyema healed after rib resection and drainage.

*Case 1.* K. II. 436/39. Male, aged 46, with bronchiectasis in the right lower lobe. For more than a year large amounts of foul-smelling sputum. 23. 3. 1939: Lobect. inf. dx. (CRAFOORD). There were broad parenchymal bridges leading to the middle and upper lobe which were treated by suturing. Profuse leakage of air from the resection surface. Suction drainage.

On the 4th day cocci and bands were cultivated from the pleural exudate. Rib resection and drainage were performed, and a communication with the bronchial tree was established which lipiodology showed to originate from peripheral bronchi in the resection surface. The wound healed without plastic manipulations.

*Case 7.* K. I. 1924/39. Male, 24 years of age, with bronchiectasis in the right lower lobe. 23. 11. 1939. Lobect. inf. dx. (CRAFOORD). A broad parenchymal bridge toward the upper lobe treated by suturing. Air oozed from the resection surface. Suction drainage.

On 16th day elevated temperature and sudden increase in sputum, up to 100—200 ml per day. On 21st day a smell exudate on a level with the anterior part of the pleural cavity was observed roentgenologically. Puncture resulted in unlimited quantities of gas. Drainage was performed.

A communication with peripheral bronchi in the parenchyma of the upperlobe (the resection surface) was later demonstrated by means of lipiodology. Healing of bronchial fistula after silver nitrate caustic.

*Case 18.* K. I. 336/42. Female, 14 years of age, with bronchiectasis in right lower lobe. Purulent sputum and intermittent haemoptyses for one year. 11. 5. 1942: Lobect. inf. dx. (LIDSTRÖM). When the lobe was being loosened a scratch was made in the middle lobe. A catgut suture was applied. Suction drainage.

One week after the operation the temperature rose and the exudate increased and became cloudy. Two months later trickling from the tube ceases suddenly. The temperature also increases and large amounts of foul-smelling sputum were coughed up. An abscess at the back of the pleural cavity was drained.

Lipiodology at a later date showed a communication with a peripheral bronchus in the middle lobe (operation injury). Spontaneous healing.

*Case 39.* K. I. 161/45. Male, 30 years of age, with bronchiectasis in the middle and lower lobes on the right side. For 10 years cough and sputum. Sputum constantly negative for tuberculosis. 12. 3. 1945. Lobect. inf. et med. dx. (CRAFOORD). Broad parenchymal bridges, connecting the upper lobe with the lower and middle ones, were treated with double rows of continuous catgut sutures. Abundant air leakage from the resection surface at the termination of the operation. Suction drainage.

The drain could not be withdrawn after the usual time. Streptococci were cultivated from the exudate. One month after the operation, pyrexia. An abscess cavity, in the wall of which there was a small bronchial fistula was drained. Bronchoscopy showed that the bronchial stump had healed by first intention. Spontaneous healing.

*There were thus no cases of insufficiency of the bronchial stump in this series.* Leakage from peripheral bronchi was on the other hand as mentioned above observed in 5 cases (Nos. 1, 7, 18, 39, 49) where it had been necessary to divide parenchymal bridges leading to residual lung tissue. In four of these cases, described in the foregoing empyema arose in connection with this procedure. The fifth case differs only in that there was no diffuse pleural infection.

*Case 49.* K. I. 941/1946. Male, 35 years of age, with bronchiectasis in the right middle lobe. 15. 7. 1946: Lobect. med. dx. (CRAFOORD). Very broad parenchymal bridges leading to the upper and lower lobes were divided and treated with double continuous catgut sutures.

A fortnight after the operation elevated temperature and increased amounts of sputum. No pleural infection. An abscess at the site of the middle lobe was drained. A communication with the bronchial tree remained which bronchography with lipiodol revealed to originate from peripheral bronchi. The bronchial stump had healed by first intention. Spontaneous healing.

Four patients died (Nos. 2, 8, 14, 28). Two of them (Nos. 8, 28, described above) died of purulent pericarditis + empyema. Case 2

died of broncho-pneumonia + cardiac insufficiency five days after the intervention. Case 14 died of cerebral oedema + mucopurulent bronchitis, also five days after the operation. In no case were inflammatory changes around the bronchial stump observed at the post mortem.

Before 1938, and also later, the bronchial stump has not been closed in number of cases according to the technique described above. Among these cases, 37 in number, empyema developed in 17 instances, and bronchial fistula in 15. Eleven of the patients died. A detailed analysis of these cases is of no interest in this connection. They should be considered as a stage in the development of this field of surgery.

### **Pleural and Mediastinal Infection.**

When the postoperative course is uncomplicated the temperature sinks slowly and reaches the normal level in 7 to 10 days. The amount of sputum immediately decreases rapidly or ceases entirely. The exudate from the pleura diminishes quickly and drainage can be withdrawn on the 4th to 10th day.

If the temperature remains high, or if it rises again at a later stage, this is due, in the majority of cases, to an infection in the mediastinum or in the pleura, but it may also be due to pulmonary complications. If the amount of sputum does not decrease directly after the operation this is usually due to a postoperative complication in the lung. If the complication disappears but the amount of sputum does not decrease, or if it increases suddenly in quantity, there is good reason to suspect bronchial leakage. If the pleural exudation does not decrease in a normal way, but is nevertheless sterile, an infection may be anticipated within a few days. If bacteria are cultivated from the pleural fluid already on the first or second day a primary infection of the pleura has taken place.

In this series the pleural infection originated as a rule from an infection in the resected lung tissue. In two cases only was the surgical operation the cause of a primary infection of the pleura. The bronchial stump and the resected lung parenchyma are always the seat of the infection. Postoperative inflammation in these parts seems to be the rule. In the majority of the cases the infection regresses spontaneously. If the bronchial stump is well closed and does not perforate despite the infection in the surroundings no bronchial fistulae will occur. The conditions were

such in all cases in this series. When the bronchial and vessel stumps are isolated from one another, as is done to protect the vessels, the bronchial stump is buried in well vascularized tissue; this will also tend to counteract infection around it.

When resection of the lung parenchyma is performed there are no such tissues at disposal for covering the resection surface. The only procedure in these cases to counteract infection is to dispose visible bronchial branches as well as possible and to apply a continuous parenchyma suture closing up the surface lightly. These cases should be primarily drained. There seems justification for wondering whether it would not be possible, as OVERHOLT suggests, not to do any parenchymal sutures in these instances and, after the parenchyma has been divided as exactly as possible in the lobar border and any bronchial branches visible treated, to allow the lobe to develop freely and hope for a rapid adhesion of the resection surface to the wall of the pleural cavity.

### Summary.

This investigation is based on a series of 53 severely infected cases of bronchiectasis from CRAFOORD's clinic. 25 males and 28 females, their ages varying between 7 and 52, average age 25 years.

Earlier reports show the importance of careful closure of the bronchial stump for the purpose of preventing postoperative infections of long duration, which often cause the death of the patient.

A short description of the diagnosis and of the preoperative, operative, and postoperative treatment is given. The bronchial stump is closed with 3 to 4 isolated silk sutures + a continuous catgut suture followed by invagination with silk and isolation from the vessels in the mediastinal tissue.

Forty-nine patients (92.4 per cent) recovered. Four deaths occurred, and are described. In no case did leakage arise in the bronchial stump. In six cases empyema developed, caused, in four of the cases, by infection from resected lung surface, in two, from primary infection of the pleura.

In five cases in which resection of broad parenchyma bridges had been done, leakage arose from the resection surface. In four of them empyema developed. All cases healed after simple drainage, without plastic manipulations.

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## On Linitis Plastica and on Sclerosing Carcinoma of the Stomach (Carcinoma disseminatum Krompecher; Carcinoma fibrosum Konjetzny).

By

KAJ RØJEL.

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Diffuse sclerosing changes of the stomach were first mentioned by ANDRAL and CRUVEILHIER at the beginning of the last century.

About 1860 BRINTON (5) gave a thorough macroscopical description of the sclerosis of the stomach, the most important characteristic of which is a considerable thickening and induration of all the layers of the stomach wall, and suggested the term "linitis plastica" for this disorder. This term proved to have a considerable vitality, but its content has been changing in the course of time.

BRINTON thought that the disease was a sclerosing of a benign nature but, gradually, in the nineties, it was realized (4) that many cases of "linitis plastica" were cases of cancer.

The problems became still more complicated, partly because a number of authors included in "linitis plastica" all sclerosing changes of the stomach, also when caused by ulcers or syphilis, or when they were components of a polyserositis, and partly because the sclerotic changes of the pylorus were confused with the pyloric stenosis in babies and with the so-called congenital pyloric stenosis in adults (16, 18).

In two pioneer works (14, 15) of 1910 and 1912 KROMPECHER drew up clear lines, stating the following division of the sclerosis of the stomach:

- 1) Congenital benign pyloric hypertrophy.
- 2) Acquired benign pyloric hypertrophy.



- 3) Acquired benign shrivelling of the entire stomach.
- 4) Acquired malignant pyloric hypertrophy.
- 5) Acquired malignant shrivelling of the entire stomach.

### Benign Sclerosis of the Stomach.

It must be considered established that benign scleroses which are not due to gastric ulcers, syphilis, or other known specific causes, occur, partly localized to the pars pylorica (7, 9, 11, 12, 17, 21) and partly comprising the entire stomach (1, 13, 14, 15). A few authors (3), however, maintain that universal scleroses of the stomach are always due to cancer, and thus deny the occurrence of the benign universal sclerosis of the stomach.

*On macroscopical examination* (1, 9, 11, 12, 13, 14, 17, 21, 22) the surface of the stomach is seen to be greyish white and opaque. The wall is firm and hard, in some cases cartilaginous; its thickness may be increased up to ten times the normal, measuring from 1.5 to 2 cm. The thickening especially affects the submucosa, to a less degree the muscularis and the serosa, and in many cases it does not affect the mucous membrane at all. The mucous membrane is well-defined against the submucosa and can be displaced. The submucosa has undergone a marked fibrous alteration and resembles tendinous or cicatricial tissue. From the submucosa numerous septa pass into the muscularis, dividing it into compartments and strands. The submucosa and the muscularis are closely connected; in some cases the border between these two layers is distinctly visible, in others it is blurred. In addition to the connective tissue proliferation of the muscularis, hypertrophy of its musculature is observed.

These changes are most frequently localized to the pars pylorica only, in other cases they take up a larger or smaller part, or sometimes the whole, of the stomach; still, they are always most marked in the pars pylorica. The delimitation in the proximal part is quite ill-defined; towards the duodenum, on the other hand, it is sharp, as the thickened pylorus projects like a portio vaginalis uteri into the normal duodenum.

*The histological picture* (9, 11, 13, 14, 17, 22) often renders possible the reading of the mechanism of development. At the initial stage an extensive oedema, in particular of the loose submucosa, is a conspicuous feature. The oedema is replaced by a granulation tissue rich in cells, which, with a constant production of fibrils,

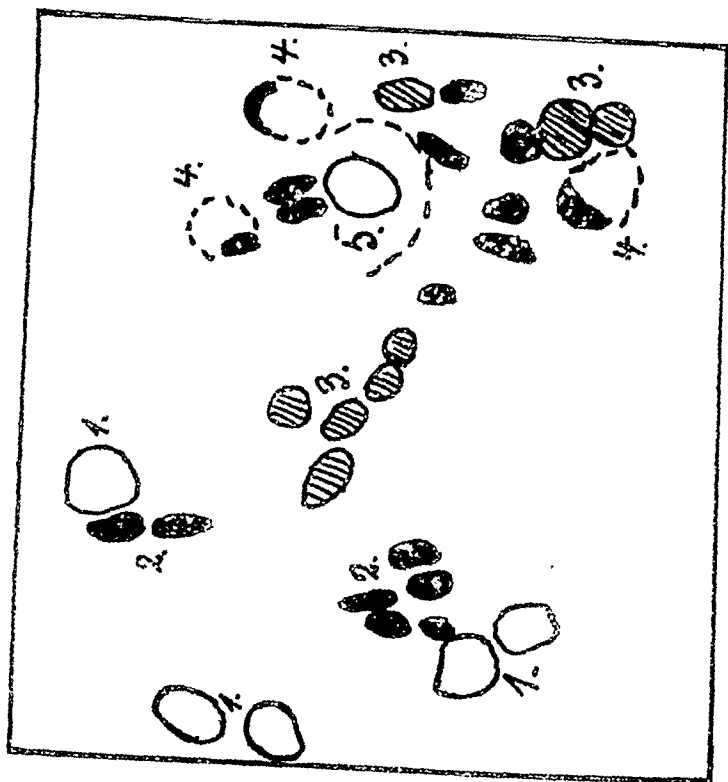


Fig. 1. Showing various types of tumour cell, marked in the drawing with figures as follows: 1) Cells with large, vesicular, ovoid nuclei poor in chromatin. 2) Cells with small, dense, ovoid rod-shaped or more irregular nuclei rich in chromatin. 3) Intermediary forms between 1) and 2). 4) Signet-ring cells. 5) Cell with bright nucleus situated in the centre, surrounding the nucleus a copious deposit of mucus in the protoplasm, which is in a state of incipient disintegration. (Fig. 1 is a high magnification of the circumscribed area in Fig. 2.)

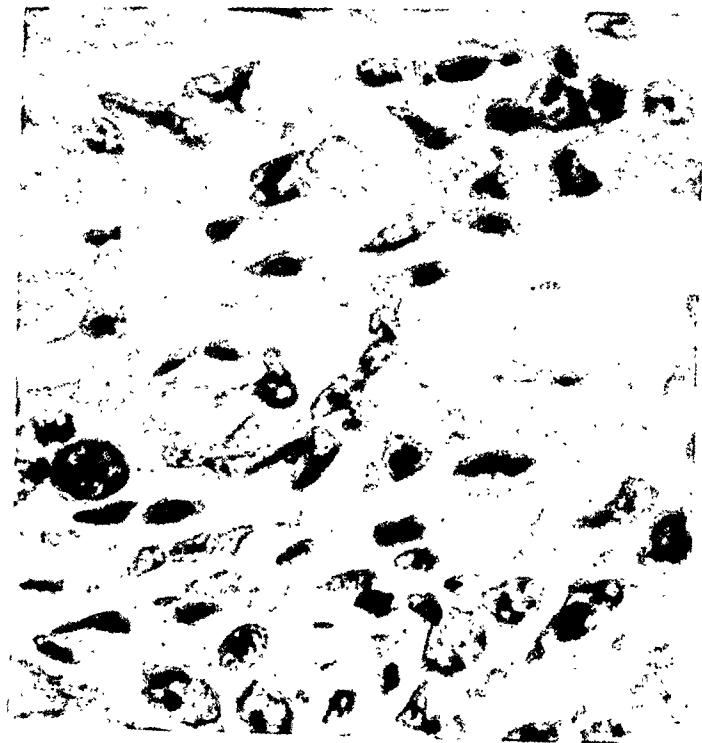




Fig. 2. Showing infiltration of the tumour in the submucosa. In the centre of the figure a cluster of tumour cells with no delimitation whatever from the oedematous stroma, into which the tumour cells spread diffusely. In right hand bottom corner a short row of tumour cells is seen in a tissue space. The large cells upwards in the centre of the figure are ganglionic cells.



Fig. 3. Showing the mucous membrane infiltrated with tumour tissue. It has displaced the glands and spread into the preformed stroma. The thickness of the mucous membrane is normal.

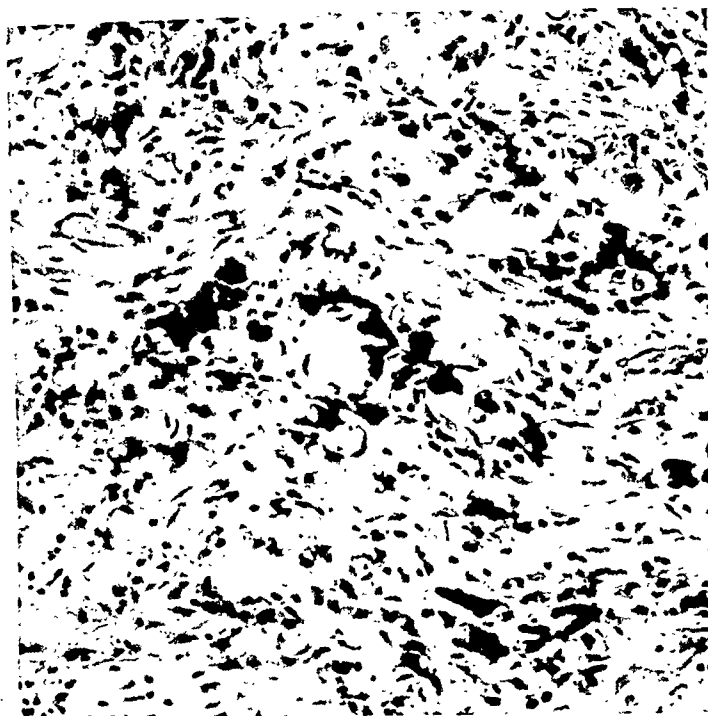


Fig. 4. Showing the submucosa with proliferation of granulation tissue and infiltration with tumour cells, some of which are signet-ring cells.

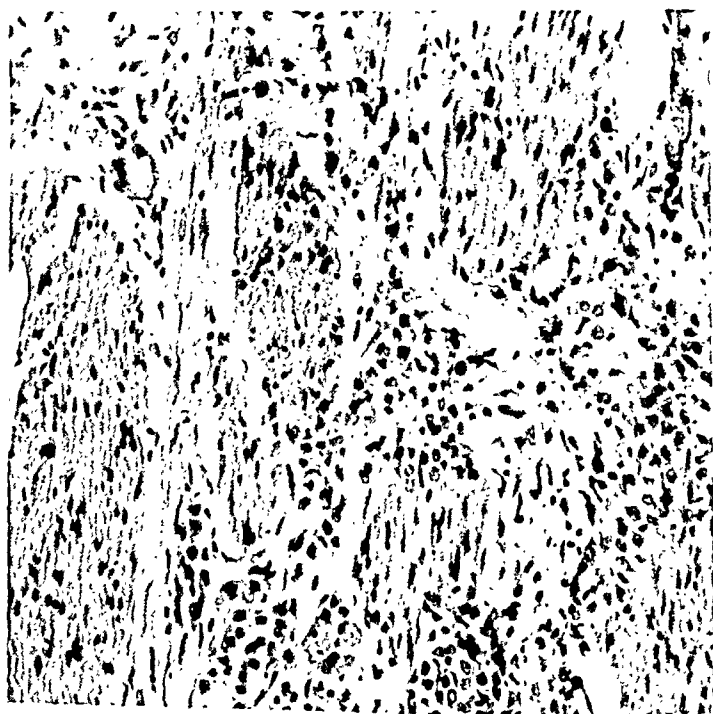


Fig. 5. Showing infiltration of the tumour between fasciculi of the split muscularis.

RØJEL: Linitis Plastica and Sclerosing Carcinoma of the Stomach.

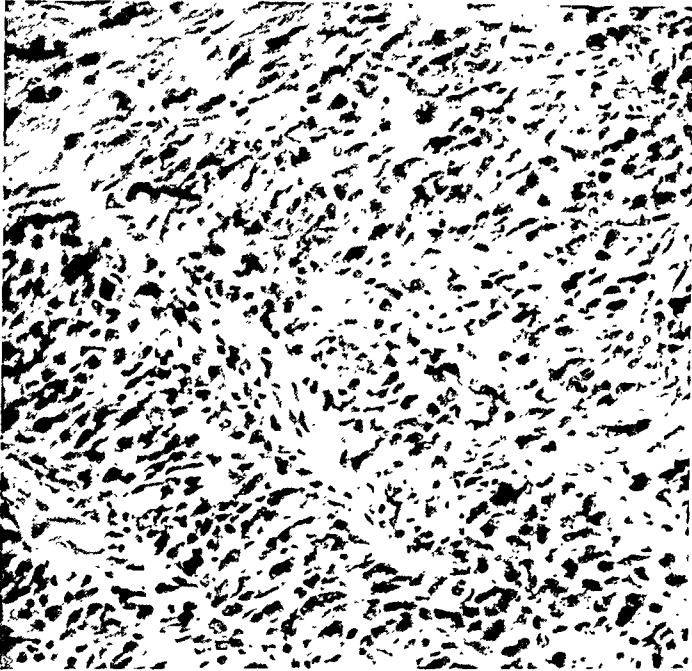


Fig. 6. Showing the muscularis with hyperplasia of the muscular cells, between which the tumour cells (most easily recognizable in centre of the figure) proliferate diffusely.

becomes increasingly poor in cells, ending at last in a hyaline fibrous cicatricial tissue which contains few cells only and which is the characteristic element of the fully developed sclerosis of the stomach.

With regard to the *etiology*, there is no agreement. It is probable that the sclerosis of the stomach may be due to disorders which, somehow or other, give rise to hyperaemia, stasis and oedema of the stomach wall: valvular disease, myodegeneratio cordis, insufficiencia cordis, arteriosclerosis of the vessels of the stomach, emphysema, adhesive pleurisy, hepatic cirrhosis and thrombosis of the portal vein (9, 12, 14, 17, 22). In some cases the sclerosis of the stomach occurs as a part phenomenon in universal polyserositis (12), in other cases the releasing cause must be supposed to be an inflammation, either a chronic gastritis or, rarely, a phlegmon of the stomach (9, 12, 21, 23). Lastly, cases have been reported in which chronic ulcers were supposed to have produced sclerosis of the stomach wall outside the areas displaying the ulcerative changes (11, 17, 21, 23).

*The symptomatology* shows nothing characteristic which may arouse suspicion of benign sclerosis of the stomach. In contrast with patients suffering from cancer of the stomach, including the diffuse sclerosing form, those suffering from benign sclerosis of the stomach have often had dyspeptic symptoms for a number of years before they develop symptoms of stenosis which lead to operation. As a rule, the roentgenologic diagnosis and the macroscopical diagnosis at operation will be cancer, and only the thorough histological examination and the further course without any metastases can clinch the diagnosis: benign sclerosis of the stomach.

*The terminology* is very copious. The following terms have been suggested to designate the sclerotic changes of the stomach: Sclerostenosis, cirrhosis ventriculi, chronic hypertrophic sclerosis of the stomach, simple inflammatory shrivelling of the stomach, fibromatosis ventriculi, stenosing gastritis etc. This abundance of terms creates some uncertainty, as it may be difficult to ascertain that the changes covered by the different terms are identical. And it is still more unfortunate that the term "linitis plastica" itself has been and is to some extent still being used to designate both the benign and the malignant sclerosing changes of the stomach.

BRINTON (5) understood by "linitis plastica" a benign disorder. When it was realized that most of BRINTON's cases were in reality

cancer, the term "linitis plastica" came to mean sclerosing cancer of the stomach (4). Later, when it was understood that a minority of the scleroses of the stomach were of a non-cancerous nature, the term "linitis plastica" was again used to designate the non-malignant scleroses.

In the more recent literature the term "linitis plastica" is used by many authors (9, 12, 13, 17, 20, 21, 22) in the sense: benign sclerosis of the stomach, while others (2, 6, 7, 8, 10) by "linitis plastica" understand cancer. Lastly, a few authors (11) use the term to describe the characteristic macroscopical picture which is common both to the benign and to the malignant form of sclerosis of the stomach, irrespective of the histological diagnosis.

Owing to the confusion caused by the indiscriminate use of the term "linitis plastica" it would perhaps be best to avoid using it altogether; if it is desired to keep this term, it would be rational to use it only to designate the benign sclerosis of the stomach.

### **Diffuse Sclerosing Carcinoma of the Stomach (Carcinoma disseminatum fibrosum Krompecher Konjetzny).**

Cancer of the stomach may be very roughly classified (3) into the following two main groups:

1) A large group in which the cancer is more or less localized, papillomatous, tumour-like or ulcerative, to which correspond the histological diagnoses of adenocarcinoma, carcinoma solidum, carcinoma colloides or mixed forms.

2) A far smaller group in which the cancerous process is diffusely spread over large areas of the stomach, ill-defined and often associated with a considerable sclerosing.

On histological examination a number of cases in this group show a parvialveolar, colloidal or adenocarcinomatous structure; they are referred by KONJETZNY (13) to a special group, termed "scirrhus ventriculi" by him.

The rest of the diffuse, sclerosing cancers display a very characteristic histological picture, which has become known in particular through the pioneer works by KROMPECHER (15) and KONJETZNY (12, 13). KROMPECHER used the term "carcinoma disseminatum"; KONJETZNY suggested the term "carcinoma fibrosum". As will appear from the description given below on the basis of the literature and of the writer's cases, this form of cancer is characterized both by the "dissemination" of the cancer

cells and by an increased formation of connective tissue. — As it seems to me that the terms of both authors have the same prescriptive right, I have joined them so as to form one term “carcinoma disseminatum fibrosum”.

In spite of its comparatively rare occurrence, this form of cancer has been quite thoroughly dealt with in the literature. This is due in particular to the protracted and comprehensive discussion as to whether the sclerotic changes were of a benign or malignant nature.

Employing quite a varied nomenclature, a great number of authors have corroborated and supplemented the observations made by KROMPECHER and KONJETZNY. In this very comprehensive literature the macroscopical and microscopical descriptions given by the various authors differ a great deal, and it is obvious that some of these cases are not completely identical with those of KROMPECHER and KONJETZNY, but that there has been a certain variation. On the other hand, the peculiarities common to different types of these sclerosing cancers of the stomach, and distinguishing them from all other forms of cancer, are so uniform and marked, and the mutual differences are so small, that the justification of collecting them in one common group is evident.

As a rule, *the macroscopical changes in carcinoma disseminatum fibrosum* (2, 3, 4, 7, 8, 11, 12, 13, 15, 19, 22, 6) set on in the pars pylorica, where they attain their greatest development. From this area they spread diffusely into the corpus and may at last effect the whole of the stomach. The delimitation is sharp at the duodenum, into which the thickened pylorus may project like a portio vaginalis. In the proximal part, the border of the pathological process is quite ill-defined; however, the histological changes generally pass on into the part of the stomach wall which, macroscopically, is apparently unaffected. When the sclerosis and the thickening are pronounced in the pars pylorica, which in that case will often assume a roundish cylindrical shape, the stomach will get a certain resemblance to a bottle, the so-called flask stomach or leather bottle stomach. — The size of the stomach varies. At the early stages, some enlargement owing to pyloric stenosis and dilation of the corpus can often be observed. As a rule, however, the stomach is diminished and shrivelled, and cases have been described in which the size of the stomach had been reduced to that of a hen's egg.

The surface is often greyish opaque and displays whitish nod-



ules, or a streaky net-like marking, corresponding to the seat of cancerous infiltrations. The consistency shows a great increase of fibrous elements and may even be cartilaginous. On the cut surface the wall is seen to be considerably thickened, in some cases up to twenty times the normal. The mucous membrane is often moderately thickened, displaying coarse, firm folds; it may be the seat of superficial ulcerations; callous ulcers are rarely seen. The submucosa is the layer that is comparatively most thickened and it displays marked fibrous changes. The muscularis, too, is thickened, partly because of hypertrophy of the musculature, partly because of increased connective tissue formation. The latter may be diffuse in some cases, in others it may occur in the form of coarse connective tissue septa between the muscular fasciculi. The borders between the individual layers are, as a rule, strikingly distinct and conspicuous. The border between the submucosa and the muscularis may, however, be blurred in parts.

As will appear from this description, the macroscopical changes in carcinoma disseminatum fibrosum are almost identical with those seen in benign sclerosis of the stomach, and it must be considered impossible to establish the differential diagnosis at the macroscopical examination.

The cancer may penetrate the stomach wall and pass on to the adjacent organs, in particular to the colon and the mesocolon transversum, which thus become fixed to the stomach.

Metastasizing to the regional lymph glands along the curvatures of the stomach is of frequent occurrence; but metastasizing to more distant parts is said to be of rarer occurrence and to appear during the late course of the disease; the peritoneum, the liver and the ovaries are particularly liable to be involved. Diffuse metastasizing simulating a systematic disorder has also been described (10).

*The histological changes in carcinoma disseminatum fibrosum* (2, 3, 4, 6, 7, 8, 10, 11, 12, 13, 15, 19, 22), which in most cases show a very considerable and rather uniform distribution, are of the same type everywhere, although the intensity of the cancer infiltration and the reactive fibrosis may be highly varying.

In some cases the typical microscopical picture of carcinoma disseminatum fibrosum can be seen in certain parts of the stomach, while in other areas the cancer is of a colloidal, alveolar or adenomatous structure; in order to exclude these cases, which do not by definition belong to carcinoma disseminatum fibrosum, the

histological examination must necessarily comprise all areas of the changed stomach wall.

The various authors give a somewhat different description of the *cancer cells*. Some authors mention large, bright and clear cells with ovoid nuclei poor in chromatin (4, 7, 8), others speak of cells with bright, vacuolated protoplasm, in which the vacuoles fuse to form a single drop which gives the mucin reaction with mucicarmine, and displaces the more rod-shaped nucleus, rich in chromatin, towards the periphery (signet-ring cells) (7, 10, 13), and others again describe cells as having rod-shaped nuclei rich in chromatin and surrounded by a scanty, ill-defined protoplasm; these cells bear a close resemblance to connective tissue cells (8, 15).

The variations in the cells described might cause some hesitation in including these forms of cancer in the same group, in spite of their other marked points of resemblance. — However, as the same stomach may be seen to contain several (8), or sometimes all (7, 13), of the variants of tumour cell described, and as it is just probable that the various forms represent different stages of development or degeneration of the same cells (7, 13), the variation of the cells referred to should not prevent the classification of these variants in one group.

The tumour cells have lost their epithelial connection and are isolated, even when situated close to one another. They do not form well-defined cords, goblets or glandular imitations, but infiltrate diffusely the host tissues, penetrating, often separately or sometimes in short chains of quite a few cells, into the tissue spaces or the lymph stream. In some cases the tumour cells are numerous and situated close to one another in clusters or strands, which, however, are always ill-defined, as a tendency to diffuse infiltration into the surroundings can always be observed along the periphery of such strands. When the cells in such clusters or strands lose their epithelial stamp, as will often be the case, the picture may resemble, and be easily mistaken for, granulation tissue (15).

The *mucous membrane* may have been completely displaced by the tumour tissue described, which, as a rule, is very rich in cells here. The reactive changes of the mucous membrane are not exactly pronounced.

Same authors (4, 7) give the following description of the mode of onset of the cancer: In the superficial layer of the, often hypertrophic, mucous membrane the glandular structure is normal. In

the deeper layers a proliferation of glandular epithelial cells takes place, whilst at the same time the delimitation of the glands from the stroma becomes blurred. The glandular tubes continue in ill-defined streaks and strands of epithelial cells, which at last lose all connections, infiltrating the stroma of the mucous membrane quite diffusely in its basal layer. It is considered to be a multicentric, universal carcinomatous degeneration of the cells of the mucous membrane of autochthonous occurrence (4, 7, 10, 13). Others (3), however, maintain that it is a cancer of focal occurrence, spreading by proliferation and infiltration in the mucous membrane.

*The muscularis mucosae* is often thickened, ill-defined and frayed and in various parts displays a diffuse penetration of the tumour cells from the mucous membrane (4, 7).

The process in the *submucosa* and the *muscularis* is characterized, partly by the tumour infiltration mentioned above and partly by the reaction of the tissues to this in the form of round-cell infiltration, development of granulation tissue and transformation of the latter into cicatricial fibrous tissue. It is striking that these different pictures of inflammation may occur simultaneously or, so to speak, mixed, so that, for example, a fibrous cicatricial tissue may be seen to contain strands of fresh granulation tissue.

In many cases the tumour cells are situated in the round-cell infiltrates or in the granulation tissue, and are thus being masked, so that they are difficult to identify; this difficulty applies, of course, in particular to the forms of tumour cell which bear resemblance to fibroblasts.

The fibrous, often hyalinized, cicatricial tissue, poor in cells, which is the result of the inflammatory changes, and which determines the sclerosis and the thickening of the stomach wall, contains, as a rule, only few tumour cells, which may be absent in large areas. KONJETZNY (12, 13) considers this to be indicative of a local "spontaneous recovery" of the tumour, which, however, continues its growth in other areas. — The fact that the tumour cells may be so scanty explains why many cases of carcinoma disseminatum fibrosum were formerly misinterpreted as benign scleroses of the stomach, and it renders necessary a comprehensive and careful histological examination before malignancy can be excluded.

*The clinical picture and the course of carcinoma disseminatum fibrosum* are not dealt with to any great extent in the literature

which chiefly deals with the pathological anatomy and histology.

I have found 8 authors (2, 4, 6, 7, 10, 11, 15, 19) who report more or less detailed case records, certain features of which may be summarily reproduced. There is a total of 25, as far as I can judge, unquestionable cases of carcinoma disseminatum fibrosum.

There were 12 males with an average of 46 years at the onset of the symptoms and 13 females whose average age was 48 years.

Detailed information is lacking in the case of 3 patients.

Five of the patients were not operated on; before their first admission to hospital they had had symptoms for 1, 5, 6, 13 and 18 months, average 7 months; they died 2, 5, 7, 13 and 18 months, average 9 months, after the onset of the symptoms.

Seventeen patients were operated on (explorative laparotomy, resection or gastro-enterostomy); in these patients the symptoms had been present before the operation for 1, 2, 3, 4, 4, 4, 4, 5, 6, 6, 9, 9, 24, 36, 60, 96 and 132 months, average 24 months.

Six out of these 17 patients died immediately after the operation; 3 died respectively 12, 18 and 21 months after the operation. Nothing is stated about the postoperative course in the remaining 8 cases.

No far-reaching conclusions can be drawn on the basis of these figures. Still, they show that carcinoma disseminatum fibrosum often comparatively soon after the onset of the symptoms takes a lethal course, and it is at any rate not the rule — as considered by KONJETZNY — that this form of cancer follows a rather benign course for a long time before becoming fatal.

With regard to the question as to how often sclerosing of the stomach is due to benign processes and how often it has been caused by carcinoma disseminatum fibrosum, or by other forms of cancer, we do not know very much. The literature on these changes of the stomach is almost exclusively casuistic, and the communications about sclerosis of the stomach caused by carcinoma disseminatum fibrosum seem to outnumber the benign forms by far. In 58 out of 60 cases of sclerosis of the stomach reported by REISCHAUER (20) the diagnosis in the histological examination was cancer. Only 2 were possibly cases of benign sclerosis of the stomach.

In this connection it may be mentioned that no cases of benign sclerosis of the stomach were observed in the material reported below.

## Writer's Cases of Carcinoma disseminatum fibrosum.

The material originates from the Surgical Department of the Odense County and City Hospital and is of the period from 1922 to 1946 inclusive. 397 cases of cancer of the stomach were diagnosed in the course of this period. In 76 of these cases, resection and microscopical examination of the stomach were made. Of the remaining number of patients — of whom 151 were not operated on, while explorative laparotomy was performed in 130 cases, and gastro-enterostomy in 40 cases — some were examined post mortem; in 3 of these post mortem examinations microscopy of the stomach was made.

During the same period (1922—1945), resection of the stomach followed by microscopical examination of the organ was made in 275 cases because of gastric or duodenal ulcer.

I have re-examined all these microscopical preparations (except a few of the first years which have been lost) and found 14 cases which it proved possible to classify as carcinoma disseminatum fibrosum in conformity with the literature referred to in the preceding pages; still, with the following reservations:

As the microscopical preparations originate from routine examinations the object of which has just been to clinch the diagnosis of cancer, sufficiently large areas of the stomach wall have not been examined in any of the cases, such as might have been desired in order to ascertain whether the cancerous process has everywhere been of the nature of carcinoma disseminatum fibrosum. It is thus possible that some of the 14 cases may have displayed the histological picture of other forms of cancer in areas of the stomach that were not examined, and ought thus to have been excluded. — It may, however, be mentioned that by far most of the preparations of the 14 selected cases contained strips of tissue of a length of several centimetres if pieced together, and originating from two or more different areas of the stomach.

As the material has been selected on the basis of the histological examination, it is most natural first to mention *the microscopical picture*.

The following description of the tumour cells and the tumour tissue is typical of all the 14 cases.

The appearance of the *tumour cells* will appear from Fig. 1 which is a high magnification of an area of Fig. 2. They often dis-

play a highly polymorphous picture but in most of the cases they can be referred to, or they constitute intermediary forms between, the following two extremes:

1) A large cell with a large round or ovoid, vesicular nucleus, mostly rather poor in chromatin, often with a distinct nucleolus (marked 1 in Fig. 1). As a rule, the nucleus appears "naked", i. e. the protoplasm of the cell cannot be observed. In some cases, however, the nucleus is seen to be surrounded by a quite bright and well-defined protoplasm.

2) The second extreme is constituted by a small form of cell whose nucleus, which is far smaller than that of the former, is dense and rich in chromatin and displays a more varied shape, from round to rod-shaped, or in some cases slightly angular (marked 2 in Fig. 1). This form of nucleus is often seen to be surrounded by a narrow and very ill-defined rim of protoplasm; quite as frequently it appears "naked". This type of cell may assume so great a resemblance with fibroblasts and fibrocytes that a distinction between tumour cells and connective tissue cells is impossible.

That these are not two different cell types, appears from the fact that an uninterrupted series of transition forms between the two extremes can be demonstrated (marked 3 in Fig. 1). I am more inclined to suppose that the larger cell type develops from the smaller one.

Both two cell forms described above and their intermediary stages display the common feature that their protoplasm may be seen to contain mucoid elements embedded which, however, can only be observed in a small percentage of a given form of cell. The mucus is seen as well-defined round "drops" in the protoplasm and stains with specific mucin-staining agents, such as mucicarmine. In the small cells the nucleus is often displaced towards the periphery, becomes flattened and assumes a crescent shape in cross sections, whilst the mucus occupies the central part of the cell surrounded by a narrow rim of protoplasm; in this manner signet-ring cells occur (marked 4 in Fig. 1). — In the larger cell, on the other hand, the nucleus, as a rule, retains its position in the centre, whilst the mucus occupies the peripheral part of the protoplasm of the cell, which thus acquires a vesicular, frothy structure (marked 5 in Fig. 1). As far as both types of cell are concerned, the terminal stage of the deposition of mucus is that the cells burst and perish, the nuclei losing their staining properties.

*The tumour tissue* (Figures 2, 3, 4, 5 and 6) displays a completely irregular and "planless" arrangement of the tumour cells, which do not show any tendency in the direction of forming glandular imitations, cords or goblets. The tumour cells infiltrate the host tissues diffusely; employing the preformed stroma, they grow into the tissue spaces, the lymph and blood vessels and along the nerves.

In some cases the tumour cells are scanty; they are then arranged separately or in short rows in the tissue spaces (Fig. 2, right hand bottom corner); they appear more frequently, however, in clusters and strands composed of many cells (Fig. 2 in the centre), but in these cases, too, it is characteristic that a delimitation of the tumour tissue is completely lacking, for along the periphery of such strands of tumour tissue the cancer cells display a tendency to merge into the host tissues.

In the following a description of the tumour infiltration and the reaction of the stomach thereto will be given for each layer separately on the basis of the 14 cases of the material. The frequency of each observation is stated in the parenthesis by the numbers of the cases in which the observation in question was made.

*The mucous membrane* (Fig. 3) was infiltrated in 12 cases (1, 2, 3, 4, 6, 7, 8, 9, 10, 12, 13 and 14) by the tumour tissue described which, however, displays a considerably greater and far more uniform abundance in cells than in the other layers of the stomach. The tumour tissue spreads by infiltration in the stroma in between the glands, causing the latter to perish gradually in the tumour tissue (3, 6, 8, 12). This may produce pictures which can be misinterpreted as a gradual transition from normal glands to tumour tissue; such a transition has, however, not been observed with certainty.

The tumour tissue may spread widely in the mucous membrane, destroying and completely displacing the glands without changing the thickness and the coarser structure of the mucous membrane. This is probably due, partly to the fact that the muscularis mucosae offers a certain resistance to the penetration of the tumour tissue, and partly to the fact that the possibility of spreading in the loose stroma of the mucous membrane is so good that local thickenings and tumour-formations are not required to give room for the proliferating tumour tissue.

In a few cases (3, 5 and 11) there are superficial, apparently benign ulcerations; their genesis and their causal relation to the tumour tissue are not clear.

The reaction of the mucous membrane to the tumour tissue is very slight in all cases, being confined to some round-cell infiltration. Proliferation of granulation tissue and sclerosing are not observed in the mucous membrane.

*The muscularis mucosae* displays considerable changes (1, 2, 3, 4, 6, 7, 9, 12 and 14). Its thickness is multiplied, and it is hyalinized, split up and with more or less blurred contours. In some parts an infiltrative invasion and penetration of tumour cells can be observed, but never so massive and so extensive that the *muscularis mucosae* perishes completely. — It does not seem to be improbable that the changes of the *muscularis mucosae* described represent a reaction against the tumour tissue aiming at preventing its growth into the deeper layers.

*The submucosa* is lacking in two preparations (10 and 11); in all the other preparations it displays the characteristic diffuse tumour infiltration already described (Figures 2 and 4). In two of the cases (4 and 6) no reactive changes can be observed. In the remaining 10 cases an often considerable reaction to the invading tumour tissue is seen. The submucosa of all ten stomachs is thickened in two cases (8 and 9) very considerably. In 3 cases (1, 2 and 14) there is a considerable and extensive oedema (Fig. 2). In 3 preparations (1, 8 and 9) there is a marked mononuclear inflammatory infiltration, and 5 cases (1, 3, 4, 8 and 9) display proliferation of fresh granulation tissue with an admixture of tumour cells (Fig. 4). Lastly, in 6 preparations (1, 2, 3, 5, 8 and 13) there are sclerosed areas in which the submucosa is poor in cells and where a hyalinized connective tissue is predominant.

*The muscularis* (Fig. 5 and 6) is lacking in one preparation (3). In all the remaining cases it has been penetrated by a typical tumour tissue. In two cases (6 and 13) it is without any reactive changes. In the remaining 11 cases the *muscularis* displays a considerable thickening; this is due to an increase both of the non-striated musculature and of the interstitial connective tissue. The hypertrophy manifests itself in two different forms which, however, may gradually pass into one another:

1) In half the number of cases (1, 4, 7, 11, 12, 14) (Fig. 5) the *muscularis* is split up into more or less distinct, often rather coarse, muscular bundles, separated by broad, most frequently somewhat loose, sometimes sclerosed, connective tissue strands. The tumour infiltration is localized in particular to the latter and shows little tendency to invade the muscular bundles.



2) In the other half of the cases (2, 5, 8, 9 and 10) (Fig. 6) there is a more intimate "blending" of the proliferating fibrous and muscular elements, so that fasciculation is either absent or not very conspicuous. In these cases the infiltration of tumour cells is, as a rule, diffuse without any localized cellular strands.

In the preparations of the 14 cases reported here the microscopical picture described appeared to be pure. However, it does not constitute any well-defined entity, as preparations of several stomachs, which have been left out of the material, displayed an admixture of tumour tissue of adenocarcinomatous, alveolar or colloidal structure in addition to the typical carcinoma disseminatum fibrosum, so that all transitions are found from the pure carcinoma disseminatum fibrosum to adenocarcinoma, carcinoma solidum and carcinoma colloides. However, when it is intended to examine the relation between the histological morphe of the tumour tissue and its biological and clinical manifestations, it is justifiable and necessary to work with "pure" histological pictures, as *in casu* those of carcinoma disseminatum fibrosum; only it should be borne in mind that this classification is an arbitrary one.

As will appear from the statements given above, there is a good correspondence between the histological picture in the 14 cases of my material and the description of carcinoma disseminatum fibrosum given in the literature, however, with the following two minor deviations: It was not possible for me to observe the gradual transition from normal glands to tumour tissue described in the literature (4, 7), or the multilocular occurrence of the tumour tissue in the mucous membrane (4, 7, 10, 13); moreover, in my material the tumour tissue seems to have been somewhat richer in cells, and the reactive sclerosis to have been less marked than corresponding to KONJETZNY's description (12, 13).

The description of the *macroscopical anatomy* in the 14 cases of the material is based chiefly on the surgeon's description of the findings at operation and of the resection preparation; a macroscopical examination by the histologist has only been made as a rare exception.

In the following 8 cases: 1, 2, 3, 6, 8, 9, 10 and 12 the macroscopical picture is typical of carcinoma disseminatum fibrosum as described in the literature.

Nos. 10 and 12 are termed "linitis plastica" without any further details.

In the remaining 6 patients there has been a diffuse, ill-defined and, as a rule, considerable thickening and sclerosing of the stomach wall, the separate layers of which could be made out very distinctly in 2 cases (2 and 8). The same two cases displayed gastritis and superficial ulcerations on macroscopical examination, whilst a third case (1) showed a mucous membrane with strikingly coarse folds. — Cancerous or callous ulcers or localized tumour-formation did not occur among these 8 typical cases. In all the 8 cases the changes were localized either to the pars pylorica alone (1, 6, 8 and 10), to the pars pylorica + the lesser curvature (2 and 12), to the pars pylorica + the lesser curvature + the greater curvature (3), or to the lesser curvature alone (9).

Mention is made of pyloric stenosis in two cases, both accompanied by enlargement and dilatation of the stomach (3 and 8).

Two cases (4 and 5) out of the 6 which could not be registered as typical are so defectively described that they cannot be classified; the case records state, however, that the pathological changes also in these cases are localized to the pars pylorica and to the lesser curvature.

The remaining 4 cases (7, 11, 13 and 14) are in the case records termed "ulcera cancrosa". Their macroscopical pictures have thus clearly differed from the one typical of carcinoma disseminatum fibrosum, although in all 4 cases the microscopical preparations were typical hereof. — In particular in these 4 cases the want is felt of the comprehensive examination of different areas of the stomach which might have settled the question whether the process occurred everywhere under the histological picture of carcinoma disseminatum fibrosum or not.

Macroscopically demonstrable metastases to the regional lymph glands occurred in Cases 4 and 6, and to the peritoneum in Case 3. Apart from this the case records do not contain any information about metastases, but in 4 cases, Nos. 2, 3, 7 and 12, it is expressly mentioned that metastases to regional lymph glands — and in 3 cases, Nos. 3, 4 and 9, that metastases to the liver — were not demonstrated.

In Cases 1, 2, 6 and 9 the malignancy of the disorder was considered doubtful at operation; in the remaining number of cases the malignancy was unquestionable already at the macroscopical examination.

In 6 cases Nos. 3, 5, 7, 10, 11 and 13, it was considered that the resection had been made through unaffected tissue; in 4 patients,

Nos. 2, 4, 9 and 14, the resection had to be made through macroscopically cancerous tissue; in the remaining 4 cases no information is given as to how radical the interference was.

*The clinical picture* in these 14 cases of carcinoma disseminatum fibrosum will only be summarily dealt with, as it does not materially differ from the well-known symptom complex characteristic of cancer of the stomach in general.

Of the 14 patients 8 were males and 6 were females, their ages at operation being: 37, 38, 43, 45, 45, 48, 52, 53, 54, 55, 55, 58, 64 and 68 years, averaging 51 years.

In the 12 cases in which the duration of the symptoms till operation is mentioned in the case records it was as follows: 2, 3, 3, 5, 6, 6, 7, 12, 12, 18, 21 and 58 months, averaging 13 months.

The frequency of the anamnestic symptoms according to the mention in the case records was as follows:

Epigastric pain .....	10 cases
Vomiting .....	9 »
including stenosis vomiting in .....	3 »
Fatigue .....	9 »
Loss of weight .....	8 »
Eructation .....	5 »
Relief from taking a meal, nausea, anorexia, inflation, alternating obstipation and diarrhoea, each .....	2 »
Obstipation .....	1 case

On examination of the patients the findings were as follows:

Palpable tumour .....	5 cases
Resistance in the epigastrium .....	2 »
Tenderness in the epigastrium .....	5 »
Emaciation .....	5 »
Pyloric stenosis (vomiting, stenotic peristalsis, large retention and characteristic X-ray findings) .....	3 »
Retention in Kemp's test meal in further .....	1 case
Constantly positive benzidine reaction in the stools .....	3 cases
Intermittently positive benzidine reaction in the stools ...	3 »
Constantly negative benzidine reaction in the stools .....	4 »
Achylia in Ewald's test meal .....	5 »
Hypochylia in Ewald's test meal .....	1 case
Normochylia in Ewald's test meal .....	2 cases

The hemoglobin percentages in the 12 cases examined were: 74, 80, 90, 90, 90, 90, 94, 95, 101, 104, 115 and 123. The sedimentation rates in the 5 cases examined were: 15, 8, 7, 7 and 5 mm.

The roentgenologic findings were as follows:

Enlarged, dilated stomach with delayed evacuation .....	3 cases
Delayed evacuation in another .....	2 »
Defective filling due to tumour .....	2 »
Narrow and rigid canalis pylori .....	8 »
including elongation of the canalis pylori in .....	2 »
Rigid area on the lesser curvature from the angulus towards the pylorus .....	1 case

In conclusion the *postoperative course* may be briefly mentioned.

One patient died on the day after the operation, and one died 15 days after the operation, the latter of subdiaphragmatic abscess.

The remaining 12 patients were discharged. 8 of them died 144, 60, 30, 24, 23, 13, 12 and 10 months after the operation. According to the statements on the death certificates, all the 8 patients died of the sequelae of their cancer of the stomach.

Four patients were still alive 22, 20, 20 and 12 months after the operation; the last-mentioned patient has later been re-admitted to hospital with unquestionable relapse.

As will appear from the case records mentioned above, it has not been possible to demonstrate biological or clinical peculiarities which distinguish carcinoma disseminatum fibrosum from other forms of cancer of the stomach and which might be related to the special histological picture. This form of cancer seems to be at least as malignant as the other forms of cancer of the stomach.

It is to be hoped that at some future date we may find remedies against this disorder to which we are at present almost unequal.

### Summary.

The writer goes over the literature dealing with benign and malignant sclerosis of the stomach. The term "linitis plastica" has given rise to much obscurity; it is suggested not to use it, or to reserve it for the benign sclerosis of the stomach. With regard to the malignant sclerosis of the stomach, it is suggested to fuse KROMPECHER's term, "carcinoma disseminatum" and KONJETZNY's term "carcinoma fibrosum", into one: "*carcinoma disseminatum fibrosum*".

The writer reports 14 cases of carcinoma disseminatum fibrosum, the histological, and to some extent also the macroscopical,

pictures of which are in conformity with the description given in the literature.

*Microscopically*, carcinoma disseminatum fibrosum is characterized by the proliferating tumour tissue and by the reaction of the stomach to this.

As far as the great majority of the tumour cells are concerned, they can be included in, or they constitute intermediary forms between, the following two types: 1) A small cell with a dense, often rod-shaped or slightly irregular nucleus rich in chromatin, and 2) a larger cell with a large, round or ovoid vesicular nucleus poor in chromatin, often containing a nucleolus.

In the protoplasm of some of these tumour cells, deposits of mucus can be observed — in the large cell type most frequently in perinuclear arrangement without displacing the nucleus, in the smaller cell, on the other hand, most frequently in the centre of the cell, displacing the nucleus towards the periphery, so that signet-ring cells occur.

The tumour cells have lost their epithelial connections and are isolated, in some cases lying separately, in others in short rows and in others again in small or larger clusters or strands, but always with a tendency to diffuse infiltration of the host tissue; they never display any formation of alveoli, cords or glandular imitations.

The reactive changes against the tumour tissue consist in mononuclear inflammatory infiltration, formation of granulation tissue and in the transformation of the latter into a shrivelled, fibrous cicatricial tissue poor in cells. Lastly, the thickening and hyalinization observed in the muscularis mucosae must probably also be considered part of the reaction of the host tissue against the tumour infiltration.

*The macroscopical picture* was typical of carcinoma disseminatum fibrosum in 8 cases: the wall was more or less thickened, shrivelled and sclerosed, in some cases with distinct borders between its individual layers, and without localized tumour-formations or callous ulcers. In 4 cases the macroscopical findings were described as cancerous ulcers, and in the remaining 2 cases the macroscopical description was too defective to allow of classification.

A brief reference is made to the clinical manifestations and the course of the 14 cases. The symptoms and the results of the laboratory examinations do not differ from those of cancer of the stomach in general. — 2 patients died immediately after the

operation. 8 patients died 144, 60, 30, 24, 13, 13, 12 and 10 months after the operation, all of the sequelae of their cancer of the stomach. 4 were still alive less than 2 years after the operation, but one of these patients is known to have a relapse.

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## Lumbar Disc Herniation.

Clinical studies and late results of 374 cases of sciatica operated on the diagnosis or suspicion of lumbar disc herniation.

Helsinki 1948. Pris Kr. 10:—.

By

WILLE WARIS.

(Autoreferat.)

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The material comprises 374 consecutive cases of sciatic pain operated at the Hospital of the Finnish Red Cross in the years 1942—45. 71 % of the patients were operated upon at the age of 30 to 49 years; 71 % were men.

*History* revealed that 29 % had had previous attacks of lumbago, 21 % long-standing back pain; the duration of the sciatic pain varied in 45 % from 1 to 5 years; 7 women stated that their sciatic trouble started during pregnancy or delivery.

*Symptomatology:* The pain was bilateral in 11 %; the Lasegue test was positive in 90 %, on both sides in 30 %. Muscle paresis was present in 3 % and weakness in the dorsiflexors of the great toe in 10 %, thrombangiitic symptoms in 5 % and in 3 cases herpes-zoster eruption in the dermatomes of the affected root. Analyzing this material it can be stated that localization of the lesion is possible by the aid of typical root syndromes in a number of cases.

*Roentgenograms* are of importance chiefly for differential diagnosis and of little value in localization. The myelographic (air myelograms) and surgical findings were similar in 68 %, and in 11 % the positive myelogram has been attributed to a disc other than that later revealed at operation.

*Operation* has been considered indicated only when conservative treatment has been of no avail. Complete laminectomies numbered

54, hemilaminectomies 187, partial hemilaminectomies 123 and transligamentary exposures 10. The spinous processes were preserved in only 11 cases. Theoretical and practical considerations relating to the extent of the exposure are presented. Radical removal of the nucleus pulposus has been performed in 151 cases and a "conservative" removal of only the herniated mass in 179 cases. In 20 % of the cases two interspaces were explored.

*Surgical findings:* Disc lesions were observed in 88 %; of these were disc herniations causing definite root compression in 77 % and in 11 % a disc protrusion was the probable cause of root compression. The negative explorations represent 12 % of the whole and include 4 % of cases where the mechanical cause of root compression may have been due to other factors.

*Late results* in 347 cases on the basis of follow-up examinations (length of observation time from 1 to 5 years) were as follows:

General results:

Completely cured .....	41 %	Working capacity	
Improved .....	50 %	Fully fit for work .....	54 %
Unchanged .....	6 %	Working capacity reduced. ....	43 %
Worse .....	1 %	Entirely incapacitated ....	3 %
Reoperated because of			
recurrences .....	2 %		100 %

(Minimum time of observation 2 years). 100 %

Radicular pain persisted:

Slight and intermittent ...	6 %
Constant, intense .....	8 %
	14 %

Back pain:

Slight and intermittent on exertion .....	24 %
Moderate or severe on exertion .....	32 %
Back pain and insufficiency even when at rest .....	10 %
	66 %

It deserves notice that the incidence of low back pain was higher than before the operation. No statistically reliable conclusions can be drawn as regards the effect of the extent of the exposure on the back pain. The late results of different authors seem to show a considerable uniformity.

Disappearance of the neurological symptoms. As late as 3 to 5 years after the operation one-half of the changes of ankle jerks still persisted. Muscle paresis had returned to normal in over



one half of the cases. Atrophy had generally disappeared from the limbs. Cramp at night was reported by 19 %; in 14 cases the patients had suffered intensely from this symptom for over three years after the operation. The thrombangiitic symptoms which 20 patients had had before the operation were considerably relieved or even disappeared completely.

A true *recurrence* at the same interspace and on the same side was not twice, once a herniation at the same level but on the opposite side, and once at the next interspace. In 7 cases reoperated because of recurring pain, no herniation was found, but all showed dense dural and radicular adhesions, which were obviously responsible for the symptoms. In 7 cases a recurrence was suspected but treated conservatively. Radical removal of the nucleus pulposus seems to give no additional guarantee against a possible recurrence of the herniation or recurrence of the sciatic pain due to cicatricial adhesions. Also in recurrences at the same interspace a considerable part of the protuberance impinging on the root consisted of scar tissue.

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### **Books Received.**

*R. Couvelaire: L'Adenomectomie Prostatique Retro-Pubienne.*  
Editions Bernard Baschet. 45 Rue De Richelieu 1948.

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From the Surgical Department of the "Karolinska Sjukhuset".  
Stockholm.

(Chief: Professor JOHN HELLSTRÖM, M. D.)

## Neurinoma in the Gastro-Intestinal Tract.<sup>1</sup>

By

JOHAN CEDERMARK †.

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Neurinomas in the gastro-intestinal tract are not of particularly infrequent occurrence; they present characteristic features which it is very important to know in order that an effective treatment may be instituted in due time. As some cases of this type have come under the author's observation at the "Karolinska sjukhuset", Stockholm, and as, moreover, several Swedish authors (BAGER, HEDLUND, LAGERGREN, NORDLANDER, SJÖVALL) have devoted special attention to these tumours it is my hope that an account of our experiences may be of some interest.

### Incidence.

During the last decades several instances of gastric neurinomas have been reported. GOSSET, BERTRAND & LOEVY presented already in 1924 in a larger account 66 cases of mostly benign gastric tumours, which proved to be neurinomas. The fact that LAGERGREN has been able to collect 14 cases from Swedish hospitals in the last decade and that in the "Karolinska sjukhuset" there have

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<sup>1</sup> Read before the "International College of Surgeons", October 1947.

It was the intention of the late JOHAN CEDERMARK to publish this work, which was to be his last, in the *Acta chir. Scand.* Feeling that no finer tribute could be paid to JOHAN CEDERMARK's memory than the publication of his own words, we, LEIF EFSKIND, JOHN HERTZ, and ERIK ROSEN, have decided to fulfil his wish. It is our hope that, on the basis of manuscripts, notes, and personal communications during his work on the subject, we have succeeded in giving this paper approximately the form which JOHAN CEDERMARK himself would have given it. We only regret the absence of some pictorial material which, unfortunately, was lost in the Bryce Canyon disaster and which we have not been able to reproduce.

been two cases since 1940, seems to suggest that they are not so very rare after all.

Tumours in the small intestine upon the whole are comparatively rare. MORRISON, *e. g.*, on an autopsy material of 13,139 found 21 cases of tumours with this localization, 13 of which were benign, and 8 malignant; the former included adenomas and neurinomas, etc., while in the latter group there were four cases of carcinoma and four of sarcoma. Among 31,331 autopsies the Swede SJÖVALL observed 70 cases of neurinoma or neurofibroma in various parts of the body, including three gastric neurinomas and two neurinomas in the small intestine. COLLINS from the period 1929—1941 collected 18 cases of neurinomas in the small intestine. Only some few cases have been published of tumours located in the caecum and the rectum. As compared to this highly infrequent location, neurinomas in the small intestine seem to be relatively common; since 1940 we have observed three cases of neurinoma in the small intestine at the "Karolinska sjukhuset". In this connection should be mentioned that in the same period we have only had two cases of carcinoma in the small intestine. In addition, from other parts of Sweden six cases of neurinomas in the small intestine have been published in approximately the same period. Fig. 1 shows the distribution of a number of gastro-intestinal neurinomas according to STOUT.

### Terminology.

The classification, pathologically, of these tumours has often presented great difficulties. In the literature the neurinoma — a name which was introduced by VEROCAY in 1910 — or allied tumours are described under such names as argentaffinoma, Schwannoma, neurolemmoma, plexiform sarcoma, fusosarcoma, etc. — For this reason it may be suspected that several cases of neurinoma have been passed by other names. ANTONI (1920), STOUT (1935), *a. o.* have given most valuable contributions to set right the concepts in this domain.

### Pathology.

These gastro-intestinal tumours are considered to have derived from Auerbach's plexus or from the submucous plexus. The

tumour is expansive in growth and most frequently well marked out. It may develop in the submucosa, displacing the lumen, or in the subserosa towards the peritoneal cavity. The larger tumours are generally coarsely lobated, surrounded by a thick connective-tissue capsule. They may be firm or soft in consistency. The cut surface often presents haemorrhagic areas, cyst-formations, or necroses.

Microscopic examination reveals a typical picture as far as the differentiated tumours are concerned. The elongated nuclei of the cell bundles are often arranged in bands resembling palisades or whirls. A more or less clearly fibrillar structure is seen in the plasma between the nuclei. The neurinomas often show a so-called micropolycystic degeneration. As these foci of degeneration increase in size and become confluent greater cavities are gradually formed in the tumour; finally, one big cavity of destruction may result. This destruction of tumour tissue explains two characteristic complications in neurinomas in the gastro-intestinal tract, viz. infection, and particularly, iteral haemorrhages. If the degenerative cavity in the tumour arises close to the mucous membrane, a perforation with a consequent haemorrhage and, in some cases, infection will often result. If the tumour, as is more rarely the case, develops in the subserosa and perforates, a peritonitis will arise. As intestinal tumours upon the whole, the neurinomas may produce an ileus.

### Symptomatology.

In tables 1 and 2 the author attempted to present the most important features of the symptomatology and diagnostics of the neurinomas in the stomach and the small intestine.

Of the *gastric neurinomas* 14 are taken from LAGERGREN's case reports. Furthermore, two of my own cases from the "Karolinska sjukhuset" have been added (table 1).

As is evident from the table the medical history often extends over several years. The most predominant symptoms have been anorexia, heartburn, acid eructations, nausea and, especially, gastric haemorrhages in the form of sanguinary vomit or melaena, often accompanied by a considerable anaemia. X-ray examination has generally revealed the diagnosis to be that of a tumour. The clinical diagnosis has often been stated as a benign or malignant tumour, without any further specification of the type. In three

Tab. 1.

*Neurinoma in the Stomach.*

Classification of LAGERGREN's cases and 2 of the author's (15 and 16).

No.	Length of case history in years	Chief symptom			X-ray	Preoperative diagnosis	Operation	Results	Special features
		Ano- rexia	Melaena or haematemesis	Anaemia Hb %					
1	1½	?	+	38	+	cancer	resection	cured	Found by chance during op. for duodenal ulcer
2	?	+	—	—	+	cancer?	resection	cured	
3	?	+	?	?	—	ulcer	resection	cured	
4	3	+	+	22	+	cancer?	resection	cured	Found at post mortem
5	2	—	+	14	+	neurinoma	excision	cured	
6	9	—	+	?	+	neurinoma	resection	cured	
7	1	—	+	?	+	?	enucleation	cured	
8	1	+	+	?	+	cancer	resection	cured	
9	1½	—	+	?	+	neurinoma	resection	cured	
10	Several	+	+	?	+	ulcer	resection	cured	
11	2	+	+	36	+	tumour	excision	cured	Peritonitis after insufficiency of suture
12	6	—	—	37	—	anaemia	no operation	died of anaemia	
13	10	+	+	50	—	anaemia	extirpation	cured	Peritonitis after insufficiency of suture
14	2 weeks	+	+	40	+	tumour	resection	died	
15	1	+	—	—	+	tumour	extirpation	cured	
16	20	+	?	?	+	tumour	resection	cured	

cases, however, the surgeon was already in advance familiar with the clinical symptoms and appearance of the neurinoma, for which reason it was possible for him to establish a diagnosis of neurinoma preoperatively with a great probability (cases 5, 6, and 9).

The neurinomas in the cases reported have only occurred in adults (aged from 40 to 82), and the incidence has been the same in both sexes. The tumours have varied in size from a cherry to an orange.

To the neurinomas in the small intestine the author has devoted a quite particular attention; in addition to three cases from the "Karolinska sjukhuset" which have been mentioned by the writer in the Swedish Surgical Society, I have, in table 2, reported a further case from Vänersborg Hospital (No. 4), which has not been published previously, and, moreover, six previously re-

Tab. 2.

*Neurinoma in the small intestine, 4 of the author's cases and 7 others from Swedish hospitals.*

Cases No. 1, 2, 3, 4 — CEDERMARK; No. 5 — HEDLUND; No. 6, 7 — BAGER; No. 8 — NORDLANDER; No. 9, 10, 11 — SJÖVALL.

No.	Length of case history in years	Chief symptom			X-ray	Preoperative diagnosis	Operation	Results	Special features
		Ano- rexia	Melaena or haematemesis	Anaemia Hb %					
1	13	+	+	55	—	Cancer coli	resection	died 6 months after operation in metastases	2 operations for ulcers
2	7	+	+	34	—	melaena	exploratory laparotomy (twice)	"	
3	8	—	+	45	—	inoperable pancreatic tumour	resection	cured	
4	—	—	—	—	—	?	extirpation	cured	Found at ileus operation
5	3	—	+	33	—	tumour in small intestine	resection	cured	
6	7	+	+	13	—	melaena	gastric resection	died	Found at autopsy
7	6	+	+	40	—	pernicious anaemia	resection	cured	
8	2	+	+	35	—	ileus	resection	died after operation	Autopsy: malignant degeneration
9	11 days	perf. peritonitis		?	—	peritonitis	resection	cured	Died 3 years later with metastases
10	?	+	+	+	—	palpable tumour	resection	cured	Incomplete report
11	?	—	—	—	—	"	"	"	Incomplete report

ported Swedish cases. These 11 cases have been tabulated according to the same principles as the gastric neurinomas (Table 2).

Remarkable of these cases is a case history extending over many years before the right diagnosis and suitable therapeutic procedure are reached. Occasional uncharacteristic digestional disturbances may occur, but the most striking feature is a trouble-



some periodical melaena causing a considerable anaemia. It has in no case been possible to make the diagnosis by means of X-ray examination, despite the fact that an examination of the passage was performed in most of the cases. Not until the tumour became palpable the diagnosis has been suspected (cases 1, 3, 10, and 11). In many cases the diagnosis and the therapeutical procedure have been instituted too late (cases 1, 2, 6, 8, and 9), even though the case history had extended over many years in some of them (Nos. 1, 2, 6, and 8). Only in one case (No. 5, HEDLUND) an exploratory laparotomy was performed on account of a melaena which had given rise to suspicion of a bleeding tumour in the small intestine.

In one case (No. 6) the tumour was only revealed at autopsy, in spite of the fact that a gastric resection had been performed previously because it was suspected that the haemorrhage originated from the stomach. In one of the author's cases (No. 1) the stomach had been operated upon twice previously, without light having been thrown upon the cause of the haemorrhage.

No more than in the gastric neurinomas does the distribution by sex and age seem to show anything of special interest. The size of the tumours has varied between a hazelnut, in a tumour which was disclosed incidentally (case No. 4), and one slightly bigger than a child's head, a tumour which showed malignant degeneration (No. 1).

It should be emphasized that gastro-intestinal neurinomas, clinically, roentgenologically, as well as pathologically, have been mistaken for myomas (case 16, table 1).

## Case Reports

of the four cases of neurinomas in the small intestine which came under the author's observation.

*Case 1.* A male, b. 1889, who in 1930 had a melaena. He was operated upon in 1931 with a gastro-enterostomy on a suspicion of gastric ulcer. Later hospitalized several times for gastric trouble and severe anaemia. In 1937 he was admitted to another hospital with a haemoglobin percentage of 35. X-ray examination showed a rapid emptying of the stomach. Reoperation was performed, with removal of the gastro-enterostomy. Later hospitalized again several times, inter alia in 1941, when x-ray examination of the stomach and colon was negative. No resistances were felt. After this he suffered from rumbling in the ab-

domen. In 1942 he himself began to feel an abdominal tumour which grew rapidly.

On October 2nd, 1942, he was admitted to the surgical department of the »Karolinska sjukhuset»; the diagnosis was cancer of the colon with metastases.

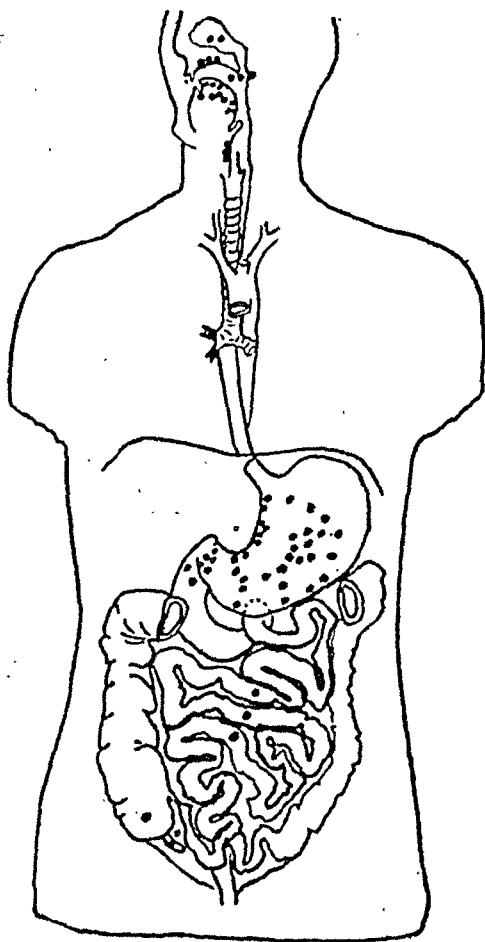


Fig. 1. Distribution of a number of gastro-intestinal neurinomas.  
(*Stout: Am. J. of Cancer, 24, 1935, p. 753.*)

On admission he presents a rather movable, firm, somewhat nodular, slightly tender tumour the size of a child's head, in the right upper part of the abdomen. Haemoglobin 60 %; red blood corpuscles 4.6 mill. Sedimentation rate 6 mm/h. Faeces: Weber's test negative. X-ray examination (October 12th) shows the tumour, which contains calcifications and seems to be of a nodular appearance, to be situated medial to the ascending colon. There is a pathologic distention of the small intestine. October 19th, 1942, an operation is performed (by the author); considerable adhesions persist from the previous operation.

A nodular tumour slightly larger than a child's head, partly soft tissue resembling cerebral tissue, partly firmer, with numerous vessels, presents itself. By successive delivery it proves to derive from a wide loop on the upper part of the jejunum; a resection of the jejunum is performed. After removal of the tumour numerous similar smaller tumours are revealed at the mesenteric root. They are removed to the greatest extent possible, but the author feels that radical removal is



Fig. 2. Extirpated duodenal neurinoma.  
(Author's observation, Case 3, Table 2.)

impossible. Pathological examination (HENSCHEN and REUTERWALL) shows a tumour very rich in cells, made up of spindle-shaped elements. Here and there polymorphism, oedema and necrosis are met with, as well as areas poorer in cells, with a distinct connective-tissue stroma. The nuclei here present a slight resemblance to palisade formation. In one place the tumour infiltrates and destroys the muscularis mucosae.

Diagnosis: malignant neurinoma (also called neurilemmoma) with metastases in the tissue removed higher up in the mesentery. No lymph gland tissue is found here.

November 6th two skin tumours on the back are extirpated. By microscopic diagnosis they prove to be structureless lipomas resembling neurofibromas.

He was discharged December 1st with the wounds healed and without symptoms subjectively. In the spring of 1943 there was a relapse of the tumour, with ascites and emaciation. He died later in 1943.

*Case 2.* A male, b. 1914. In 1939 he had indigestion and melaena. He was admitted to the hospital as a gastric ulcer was suspected. No resistances could be felt in the abdomen. He had melaena, and the

haemoglobin percentage was 34. X-ray examination of the stomach and the duodenum was essentially negative. He was first treated in the medical department, but later transferred to the surgical department on an uncertain diagnosis. An exploratory laparotomy is performed on September 7th, 1944. The stomach and the duodenum show normal conditions; on closer examination a tumour the size of a tangerine and surrounded by large vessels is revealed on the posterior wall of the descending part of the duodenum. A radical operation is attempted

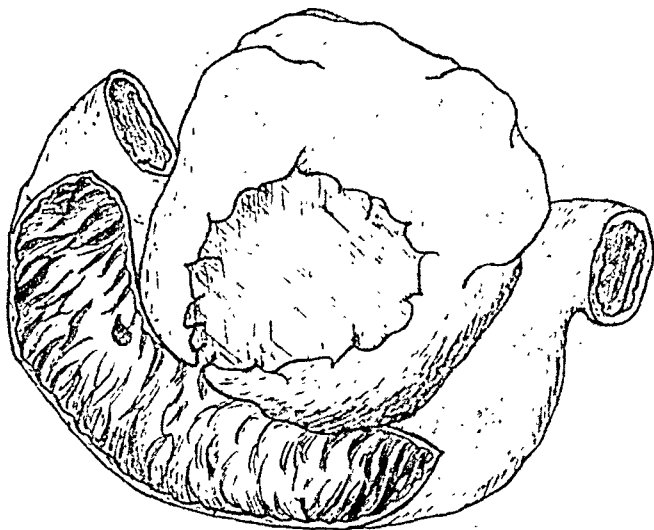


Fig. 3. Schematic drawing of a neurinoma in the duodenum.  
(Author's observation, Case 3, Table 2.)

without success; the surgery has to be confined to taking a biopsy. The postoperative course is uneventful.

Pathological examination (REUTERWALL) reveals a neurinoma rich in cells, in some places with nuclei arranged like palisades. Some nuclear polymorphism, occasionally with hyperchromatism, and some few mitoses. The tumour is partly surrounded by coarsely lamellated tissue. This connective tissue is in some places infiltrated and destroyed by the tumour. There are no symptoms to support a diagnosis of sarcoma in the strict sense of that word, but the specimens suggest a local malignancy. Diagnosis: Neurinomatous tissue, rich in cells, partly with so-called local malignancy.

November 10th, 1945, he was admitted to the medical department of the »Karolinska sjukhuset» for permanent melaena. The haemoglobin percentage was 45, the sedimentation rate 61 mm/h. The liver could be palpated 3 fingerbreadths below the costal margin. He was given X-ray treatment. February 21st, 1946, he was transferred to the surgical department for reoperation. A new exploratory laparotomy was performed (JOHN HELLSTRÖM). In the hilus of the liver and the liver

proper some rounded larger and smaller tumours were found. Through the duodenum a diffuse nodular tumour, which had clearly given rise to metastases, could be felt. He was discharged from the hospital March 2nd, in comparatively good general condition. He died in July 1947.

*Case 3.* A female, b. in 1893. In 1938 she suffered from anaemia and fatigue. Since 1944 she has had stitches and tenderness in the right part of the abdomen. From February 1946 she has suffered from fainting fits, vomiting and eructations. The haemoglobin percentage was 45. A tumour the size of an orange could be palpated in the right part of the epigastrium. X-ray examination (February 26th, 1946) revealed no changes in the stomach and duodenum, the diagnosis was a pancreatic tumour. March 4th, 1946, an exploratory laparotomy was performed, but as the tumour was considered to be an inoperable pancreatic neoplasm further surgery was desisted from.

She was admitted to the »Karolinska sjukhuset», surgical department, May 29th, 1946. A comparatively firm resistance the size of a fist is palpated in the right part of the epigastrium. The haemoglobin percentage is 60. X-ray examination reveals a dislocation by a retroperitoneal tumour of the descending part of the duodenum in a curve anteriorly and somewhat to the left. There are no signs of growth of the tumour into the duodenum.

By operation June 20th, 1946, (by the author) a retroperitoneal tumour, slightly larger than a fist, located posterior to the duodenum presents itself. Over the tumour there are numerous dilated vessels. By lateral division of the peritoneum a comparatively well defined tumour is revealed which can be pared from the surrounding soft tissues until it presents itself to be intimately connected with the descending part of the duodenum, for a stretch of 4 cm. involving more than half of the circumference. A portion of the descending part of the duodenum is resected with the tumour (Fig. 2). A mesenteric gland the size of a finger tip, close to the tumour, is removed. The specimen shows the duodenal lumen to be connected with the interior necrotic part of the tumour by a deep crater. (Fig. 3, schematic drawing.)

Pathological examination shows a typical neurinoma which originally seems to have been derived from the muscularis, after the partial destruction of which it has reached the muscularis mucosae and the luminal mucous membrane, here presenting a deep necrosis and granulation tissue. There are no signs of malignancy but areas suspected of destructive growth. The removed gland presents hyperplasia but no symptoms of tumour growth. Diagnosis: Neurinoma.

*Case 4.* A male, b. in 1906. He was operated upon in Vänersborg Hospital for ileus due to a Meckel's diverticulum. At the same time a tumour the size of a hazelnut was incidentally discovered in the jejunum. The tumour is removed. It is a typical, well defined neurinoma, which so far has not had the time to give symptoms. The microscopical specimen gives, however, suspicion of destructive growth.

### Discussion.

The author's first three cases have had a protracted course. In the first case the diagnosis is only made after 13 years, in the second case after 5 years and in the third after 8 years. There is reason to believe that the first case has started as a benign neurinoma which has later become malignant and given rise to metastases. The same holds good for the second case. This is a striking fact, as neurinomas generally are benign and are reported in the literature to metastasize but very rarely. In the third case the tumour is clearly still benign but has, by its necrotic tendency, given rise to severe clinical symptoms. The fourth case has not yet had the time to give any symptoms.

In other cases reported in the literature of neurinomas of the small intestine, benign as well as malignant, the symptoms from the tumour, apart from melaena, must be ascribed to a peritonitis due to a perforation from the necrotic cavity to the peritoneum, as in one of SJÖVALL's cases (No. 9), or to an ileus caused by the tumour, as in NORDLANDER's case (No. 8).

The symptoms, consequently, are most frequently caused by iterated haemorrhages in cases of gastric neurinomas as well as neurinomas in the small intestine. When the tumour is located in the stomach the diagnosis can most frequently be made by means of X-ray, which has not so far at any rate been able to establish any diagnosis in cases of neurinomas in the small intestine. In such cases of occult melaena an exploratory laparotomy is the only way to display the diagnosis.

Even if a gastric neurinoma or a neurinoma in the small intestine is benign, it may give rise to fatal complications, as haemorrhage with resultant anaemia, to peritonitis or ileus, or a neurinoma which is originally benign may become malignant.

A favourable prognosis may generally be expected by removal of the tumour through extirpation or resection at a sufficiently early stage of the disease.

### Summary.

An account is given of the incidence, pathology and clinical symptoms of the neurinomas in the stomach and the small intestine, based on a material comprising two cases of gastric

neurinoma observed by the author, and fourteen from other Swedish hospitals; further, four neurinomas of the small intestine and six from other Swedish hospitals. Pathologically the tumours are described as having derived from Auerbach's plexus or the submucous plexus. In the clinical account the long duration of the disease is emphasized as well as the haemorrhages, especially in the form of melaena which may give rise to a considerable anaemia. An X-ray examination may be an aid in the diagnosis of a gastric neurinoma but has in none of the cases of neurinomas in the small intestine been of any help. The tumours may give fatal complications, as severe anaemia, peritonitis and malignant development. The treatment is surgery which, when instituted early, may give a good prognosis.

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# A Contribution to the Knowledge of Primary Genital Tuberculosis with a Venereal Basis.

By  
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In 1920 BAUEREISEN showed experimentally that tuberculosis inoculated into the seminal vesicles of guinea-pigs was transmitted from these and gave rise to tuberculous disease of the genitals of the female.

GOHN and KAPTA stated in 1926 that transmission of primary genital tuberculosis between humans upon coitus is improbable, although not inconceivable.

HELLERSTRÖM in 1939 called attention to the occurrence of primary genital tuberculosis with a venereal basis. In his study he describes in detail a personal case of primary tuberculosis in the genital organs of a woman inoculated upon coitus with a man suffering from urinary tract tuberculosis in whose urine the presence of tubercle bacilli was unquestionably established, and an analogous case from CHEVALLIER, COLIN, KAPLAN, and ORINSTEIN. He further describes a case of ROCHAT, which, however, was interpreted by the latter as a superimposed tuberculous infection with a so-called pseudoprimary complex in the female genitals. In addition to the cases mentioned above the author has found in the literature a case published by SCHMID in 1940. That contamination also may be transferred in the opposite direction, *i. e.* from female urinary tract tuberculosis to the male genitals, is shown by a case described by STRAND in 1945. The present paper describes a case of tuberculous infection from male to female observed by the author. A table including



all of the cases known to the author is presented as well as a short epicrisis of the present case.

*23-Year-Old Female. Dairy-Shop Employee.*

The patient on 1. 16. 1942 came to the author for advice for acute fever with swelling of the groins.

*Anamnesis:* Dry pleurisy 11 years earlier. Chest X-ray 2 years after the pleurisy not remarkable. In connection with her employment at the dairy shop Mantoux 1 mg negative, 12. 21. 1940 (Dr. B. SUNDLÖF, Gefle). Menses regular with a duration of 6 days and an interval of 28 days. Last menses 12. 31. 1941. Genital discharge of several years standing. Aggravated since the beginning of December. Has had intercourse twice in her life, on 11. 22. and 12. 13. 1941, both times with the same man.

The patient has been ill since 1. 5. 1942 with headache and fever which on 1. 8. was 39° C, on 1. 15. 37.9°—38.2° C, and on 1. 16. 38° C. Initially she had a slightly sore throat, later stiffness at the back of the neck and an increasing swelling in both groins, the latter aching relatively little. There was a hacking cough.

*Status.* 1. 16. 1942: General condition good. Well nourished. Flushed and feverish. Temp. 38.2° C. Heart: 0. Lungs: 0. Abdomen: 0. Local examination: in the right groin above Poupart's ligament corresponding to the lower portion of the inguinal canal a lymphadenitis the size of a hen's egg was observed. In the same site on the left side there was a lymphadenitis the size of a walnut. These were both rather tender. No unquestionable fluctuation was established and the overlying skin was normal. Marked intertriginous eczema around the vulva and anus. Vaginal examination: uterus could not be defined; no resistance palpable in the true pelvis. The examination was rendered very difficult by pain localized by the patient to introitus vaginae. Speculum examination: vagina fiercely red, with an abundant thin yellow secretion. Portio not remarkable. Clear mucus in the external orifice of the cervix. Posteriorly in the hymenal ring an unhealed lesion (unhealed laceration?). Smears from cervix and the urethra: 0 gonococci. From the vagina: streptococci.

*Diagnosis:* Intertrigo in the ano-genital region + acute colpitis + acute lymphadenitis of the bilateral inguinal region.

*Treatment:* External washings with a weak solution of potassium permanganate + dialon powder. Sulfonamide 0.5 g.  $\times$  5. Bed-rest. Temp. 1. 17.: 36.6°—38.1° C, 1. 18.: 37.5°—37.7° C, 1. 19.: 37°—37.4° C. At examination 1. 20.: afebrile, adenites decreased in size, intertrigo nearly cured. Speculum examination: ulceration in hymenal ring not healed. Vagina still fiercely red. Vagina painted with 3 per cent hydrogen peroxide, 5 per cent lapis solution, and normolactol.

At examination 1. 23.: afebrile, intertrigo healed. Speculum examination: posteriorly in the hymenal ring an irregular ulcer the size of a pea, right edge rather undermined, base of the lesion rather soft. No edema in the labium majus. Vaginal smears: streptococci.

When seen 1. 29. the patient reported that since 1. 28. she had had tender nodes on the leg. Status 1. 29.: on both lower legs, especially the left, rather raised, round, bluish-red tender infiltrations about 2½ cm in diameter. Intertrigo healed. Pirquet: vesicle about 1½ cm in diameter surrounded by a red zone 1 cm wide.

Chest: 0.

Temp. between 2. 1.—2. 13.: morning temp. max. 37.4° C, evening temp. max. 37.7° C, from 2. 10. entirely normal.

X-ray examination 2. 2. 1942: "lungs: thorax bilaterally equal in size. Absence of mediastinal shift. Diaphragm and sinus not remarkable. No changes observed in the hilar region, pulmonary fields or pleurae." (Dr. STIG LINDHOLM, X-ray Department, Central Hospital, Gefle.)

2. 6.: Afebrile, felt stiff in the joints. S. R. 23 mm. Ulceration in hymenal ring unchanged. Vagina not remarkable. In the right groin a fluctuating gland, rather larger than a walnut was observed under bluish-red skin; in the left groin a similar gland the size of a hazel-nut. Puncture of right adenitis: 1 cc. of tbc-like pus. Smear: methylene blue stain: abundant pus cells. 0 bacteria. Specimen of pus sent to the bacterial laboratory of the Sahlgren Hospital, Gothenburg, for guinea-pig inoculation. Report 2. 11.: "pus from inguinal gland. Direct preparation: abundant tubercle bacilli." (Dr. A. WASSÉN, Gothenburg.) This report was later supplemented by the statement that the pus from the inguinal gland was found on culture to contain tubercle bacilli of human type.

In view of the above facts the author now considered it justifiable to change the diagnosis made 1. 16. to primary tuberculosis (tuberculous ulcer of the hymenal region + bilateral tuberculous lymphadenitis of the inguinal region + erythema nodosum). This diagnosis was strongly substantiated by information from the records of the male from the surgical department of the Central Hospital, Gefle.

During the period 2. 13. to 3. 14. repeated punctures of the adenitis. S. R. 2. 21.: 26; 3. 7.: 28. Discomfort in articulations at first persistent, but after treatment with 1 g. of sodium salicylate  $\times$  3 this cleared up entirely by 3. 14. On 2. 21. the sore in the posterior of the hymenal ring the size of a navy bean, with undermined edges and a rather indurated base.

3. 21.: Incision and curettage of the right adenitis. 4. 9.: X-ray treatment of the adenites initiated. 4. 23. a triangular ulceration the size of a grain of rice found in the posterior midline of the hymenal ring. Application for admission to the Coast Sanatorium was made, but the patient was not accepted. 5. 7.: S. R. 13. 6. 2. she felt very well subjectively; the adenites were in satisfactory regression. 9. 7. the hymenal lesion had the same appearance as 4. 23. The left adenitis was the size of a navy bean. The right adenitis was again curetted. 7. 15. 1942: X-ray examination of the lungs at the Central Dispensary in Sandviken showed nothing remarkable. 9. 4. the inguinal adenitis was about the same as 7. 9.; a rightsided fistula was curetted. The general condition was very good. From 7. 14. the patient was at work full-time. 10. 23.

the ulcer in the vulva was about the same as previously, while the fistula in the right groin had contracted satisfactorily. The left groin was unchanged.

The author now did not see the patient until 4. 13., 1943. She had then had a stitch in the right side on respiration since about 4. 8. On 4. 9. she had a temperature of  $39.1^{\circ}$  C. 4. 11.: afebrile, 4. 12.:  $38^{\circ}$  C, 4. 13.:  $36.9^{\circ}$  C.

*Status:* General condition very good. Chest: 0 dulness, retraction on right side, respiratory sounds normal. In right groin 2 small fistulas, in left groin an indurated non-tender adenitis, easily movable, the size of a hazel-nut. S. R. 38 mm.

*X-ray examination:* 3. 15. 1943: "right-sided small pleural exudate of serous type. Supraclavicularly on the right side small flecks of suspicious appearance; otherwise no pulmonary foci demonstrable. On the left side no obvious changes. *Diagnosis:* "right-sided exudative pleuritis" (Dr. S. ARNELL, Central Hospital, Gefle.)

The patient was at first referred to the medical service of the Central Hospital, Gefle, and thence to the Jonas Selggren Sanatorium, Gefle, where she was treated from 4. 30. to 8. 13. 1943 (Record No. 53/43).

*Diagnosis:* Right-sided exudative pleurisy + tuberculosis of the introitus vaginae + tuberculosis of the inguinal lymph-glands.

*Anamnesis:* Had felt well all winter and spring. About 4. 8. onset of fever and a stitch in the right side. Admission to the medical department of the Central Hospital, Gefle, 1 week after onset. Puncture gave negative findings. She had a temperature of  $39^{\circ}$  C, soon subsiding to  $37^{\circ}$ — $37.5^{\circ}$  C. Slight cough. 0 expectoration. 0 hemoptysis.

*Status:* General condition good. Lungs: diminished action of right lung. Local examination: a non-tender gland the size of a hazel-nut observed in the left groin and a similar gland and small scar in the right groin. In the posterior margin of the introitus was found a small ulcer with a sticky coating.

*X-ray examination* upon admission: right diaphragm raised. Sinus region adherent. A slight, streaky density, probably pleural in origin, observed in I 2. Left side 0.

0 tubercle bacilli in repeated examination of sputum, stomach washings + culture upon admission and discharge. S. R. on admission 12; discharge 5. X-ray examination on discharge: status quo.

6. 10.: Incision of right groin.

6. 30.: Primary ulceration healed. Persisting secretion from the lymphadenitis in the left groin.

7. 29.: Slight secretion. 8. 10.: open fistula with secretion still in left groin. Glands small, non-tender, firm, twice the size of a bean.

9. 1. 1943: The patient was again seen; the right groin was healed without deep infiltration. On the left side there was a small fistula, absence of infiltrations. The lesion in the hymenal ring was healed. Speculum examination: not remarkable. S. R. 11 mm.

The patient had not yet begun to work when the author was called in 10. 17., because of the onset, 2 days earlier, of a stitch in the left side of the chest. The patient exhibited symptoms of left-sided exuda-

tive pleurisy and was referred to the Jonas Selggren Sanatorium, Gefle, where she was treated from 10. 19. 1943 to 4. 15. 1944 (Record Nr. 121/43).

*Diagnosis:* Left-sided exudative pleurisy + sequelae of right-sided pleurisy + tuberculosis of the inguinal lymph-glands + tuberculous osteochondritis of the left fifth rib.

*From the anamnesis:* Acute onset 10. 16. with stitch in left side. Temp. 39° C.

*Status:* General condition rather poor, tired, some dyspnea. Pulse rate 130. Lungs: decreased respiratory sounds, although distinguishable at the left apex, and dullness.

*X-ray examination* 10. 19.: Right sinus region filled; otherwise nothing definite on the right side. Below left C 4 diffuse veiling, increasing towards the base. Diaphragm not visualized, nothing definite in the parenchyma. Thoracocentesis 500 cc.

0 tubercle bacilli in culture on admission and discharge. S. R. on admission 35; discharge 10 mm. 11. 20.: no fistulae in groin. The patient reported tenderness for some time over the sternum. A tense induration felt at the insertion of C 5 at the left side of the sternum. 2. 12.: incision of tumor at hospital. Abundant thick pus. *Diagnosis:* tuberculous osteochondritis. 3. 2. 1944: well. Ulceration in vaginal introitus healed and covered with normal mucosa. No palpable glands in the right groin. A couple of pea sized glands in the left groin. Ulceration over cost. V now only about the size of a penny, with slight secretion.

*X-ray examination* 4. 15.: No visible parenchymal changes. Right sinus adherent. Thin veiling above the raised left diaphragm. Otherwise nothing remarkable.

6. 16. Small ulceration remaining over the costae. No palpable glands in groin. Patient permitted to work.

10. 5. Persistent small fistula with scanty secretion.

2. 27. 1945. Patient at work in shoe-shop. Fistula on chest healed. S. R. 9 mm.

5. 31. Patient well since last examination but the fistula on her chest opened about a week before. Working full time. S. R. 10 mm.

#### *Source of Infection. 23-year-old Travelling Salesman.*

11. 30. 1940 left-sided epididymectomy for left-sided tuberculous epididymitis. 6. 11. 1941 right-sided nephrectomy for tuberculosis of the kidneys. Tubercle bacilli established in urine 5. 19. and 5. 23., 1941. Guinea-pig test of urine from the left ureter positive for tuberculosis, human type bacilli. Cystoscopy 5. 16. 1941 showed changes of the bladder which were suspected to be tuberculous in nature. 2. 16. 1942 tubercle bacilli again established in the urine and guinea-pig test of urine 2. 6. 1943 positive for tuberculosis, human type. All reports derived from the records of the surgical department, the Central Hospital, Gefle (Record Nos: 2031/40, 932/41, 81/43, 385/44).

Thus it was hereby fully established that at the close of 1941 the man in question had urinary tract tuberculosis with tubercle bacilli of human type in his urine.

Table  
*Primary venereal genital*

No.	Age	Symptoms	Period of Incub.	Disease of Source of Infection
1	20 yrs.	Ulceration post. in hymen + lymphadenit. supp. inguin. bil.	Appr. 6 weeks prior to adenitis.	Orchitis & epididymitis tbc.
2	22 yrs.	Ulceration at orifice of left Barthol. gl. + lymph. caeos. ing.	3—4 weeks prior to adenitis.	Tbc. ren. et ureter. Nephrectomy + ureterolithotomy 8½ months prior to infect. coitus.
3	23 yrs.	Ulceration post. in hymen + lymphaden. supp. ing. Eryth. nodosum. Bil. exudat. pleurisy. Osteochondrit. tbc.	Either 44 or 23 days prior to onset. 67 or 36 days prior to eryth. nod. Appr. 16 months & 23 months prior to pleurisy. Appr. 2 years prior to osteochondritis.	Epididymit. tbc. dxt. Tbc. ren. bil. Cystitis tbc? Epididymectomy dxt. + nephrectomy dxt. prior to infect. coitus.
4	28 yrs.	Ulceration post. in vulva (hymen) with indurated base + lymphadenit. ing. bil. caeosa.	Appr. 1 month prior to fever and adenitis.	Tuberculous osteitis in right ankle + prostatitis + spermato-cystit. tbc. dxt.

### Epierisis.

Of especial interest are the site of the primary lesion in the hymenal laceration, its tenderness, and also the induration of the base of the lesion at a later stage, which might give rise to difficulties in differentiation between tuberculosis, luetic primary effect, and cancer, as was also pointed out in works by BRUUS-GAARD and STRAND on tuberculous primary lesions in the genital organs.

The exact interval between the infecting coitus and the appearance of the symptoms in the female — the incubation period of the tuberculous disease — may be given as 44 days or 23 days, dependent on the occasion on which the infection was transmitted. Between inoculation and the appearance of the erythema nodo-

## I.

*tuberculosis in the female.*

Tubercle Bacilli	Prognosis	Remarks	Authors	Date of Observation
In adenit. of female. In urine of male.	Regression.	Deflor. in conn. with coitus.	CHEVALIER, COLIN, KAPLAN & ORINSTEIN.	Oct. 1936.
In female's adenitis & ulceration. Guinea-pig test of male's urine pos. for tubercle ba- cilli.	Recovery af- ter appr. 2 years.	Deflor. in conn. with infect. coitus.	HELLER- STRÖM.	Dec. 1936.
In adenitis of female. In male's urine be- fore and after coi- tus.	Complica- tions: cf. symptoms. Recovery after 3½ years.	Deflor. in conn. with coitus.	NILSON.	Jan. 1942.
P. A. D. on female's adenitis: T. B. C. Guinea-pig test: of female's urine: Neg.; of male's urine after coitus: Pos.	Regression.	Deflor. at in- fect. coitus.	SCHMID.	1939

sum there was an interval of 67 or 36 days. After about 1 year and 3 months the right-sided pleurisy set in, after about 1 year and 11 months the left-sided pleurisy, and after about 2 years the osteochondritis.

It is pointed out that the pleurisies appeared without any sign whatsoever of pulmonary or hilar gland tuberculosis.

From the point of view of Swedish tuberculosis treatment it is remarkable that this woman was not a case that could be received at the Coast Sanatorium for treatment of her primary tuberculosis, a treatment which perhaps might have improved her prospects of avoiding the complications that later occurred. (LJUNGGREN has also called attention in a study to the fact that urinary tract tuberculosis is not received for after-treatment at coastal sanatoriums either, as is to be desired.)

Table  
*Pseudoprimary venereal genital*

No.	Age	Symptoms	Period of Incub.	Disease of Source of Infection
1	21 yrs.	Ulceration post. in hymen + lymphadenit. supp. bil.	3—4 weeks prior to adenitis.	Epididymit. tbc. bil. "Castration" on left side appr. 2 months prior to first coitus.

Table  
*Primary venereal genital*

No.	Age	Symptoms	Period of Incub.	Disease of Source of Infection
1	40 yrs.	Ulcer in sulcus coronarius + adenitis in groin.	At least 3 weeks prior to adenitis.	Tbc of left kidney and ureter.

The woman would have been protected from this tuberculous infection involving such protracted illness and incapacity for work if the man in question had had knowledge of the contagious nature of his urinary tract tuberculosis and of the necessity of using a condom in order to prevent the spread of infection. The author has not been able to find mention in the literature of this possibility of avoiding infection from urinary tract tuberculosis.

It appears from the tables that all cases of infection transmitted to females are such that the infection has with certainty been inoculated into the hymenal lesion that occurred at defloration. It therefore appears as though female tuberculin-negative virgins especially were susceptible to tuberculous infection via this route.

It does not seem improbable, as pointed out by HELLERSTRÖM, that primary tuberculosis, venereally transmitted, is less uncommon than ordinarily believed. Clear cases of this type are perhaps rare owing to the difficulties of diagnosing a lesion located higher up in the female genital tract and thus connected with intra-abdominal lymph-glands. With the diminished tuberculosis morbidity in Sweden the prospects of reaching adulthood without

## II.

*tuberculosis in the female.*

Tubercle bacilli	Prognosis	Remarks	Author	Date of Observation
In adenites of female. Guinea-pig test of male's urine pos. 2 weeks prior to castration.	Recovery after 14 months.	Deflor. in conn. with coitus.	ROCHAT.	?

## III.

*tuberculosis in the male.*

Tubercle Bacilli	Prognosis	Author	Date of observ.
In male's adenitis. P. A. D. of his ulcer: TBC. TBC Bacilli in female's urine after coitus.	Regression.	STRAND.	1943

previously having been infected with tuberculosis are greater, with a consequently augmented risk of infection by this route. Also, the possibility of a superimposed infection in an individual already infected can not be excluded, although it is not easy here either definitely to establish that the genital tuberculosis was transmitted venereally. That this does occur, however, may be indicated by the case of ROCHAT.

In the Swedish literature LJUNGGREN has pointed out the relatively common incidence of urinary tract tuberculosis so localized that it cannot be treated with radical surgical intervention, *i. e.* in the prostata and the seminal vesicles. He calls attention to the great risk of recidivation and the high late mortality in tuberculous epididymitis, and also to the fact that about 75 % of the patients with the latter disease have concomitant tuberculosis of the prostata and the seminal vesicles, while among the remaining 25 per cent a number have tuberculosis in the rest of their urinary tract. It is therefore strongly emphasized that it should be the physicians duty in every case of urinary tract tuberculosis to recommend the use of condoms as a prophylactic measure against the dissemination of infection by this route.



## Summary.

### *On Primary Genital Tuberculosis as Venereal Disease.*

In the present paper 3 cases from the literature and a personal case of primary tuberculosis in the vulva inoculated from a male subject with urinary tract tuberculosis are described. In all of the cases inoculation occurred in the hymenal laceration at intercourse. One case with inoculation from a female with urinary tract tuberculosis to the male genitals under similar conditions is also described. A number of diagnostic and social aspects are discussed. Such cases are possibly not so infrequent as is generally believed, due to diagnostic difficulties. They also suggest the possibility of tuberculous superinfection especially in the female genitals, although here definite proof of the incidence of fresh infection and of its source in the urinary tract tuberculosis of the partner can never be given. The possibility of avoiding such tuberculous contamination by the employment of condoms is pointed out.

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From the Rudolph Bergh, Hospital, Copenhagen.  
(Chief: AA. KRISTJANSEN, M. D.)

## Tetanus Following Burns.

### Report of a Fatal Case in Spite of Prophylactic Antitoxin and Penicillin Treatment during the Period of Incubation.

With a Few Statistical Remarks on the Estimation  
of the Prognosis in Tetanus.

By

AXEL PERDRUP.

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Tetanus is rarely seen following burns. Among 527 cases of tetanus in Denmark during peacetime (5) only two were caused by burns. Moreover, tetanus seldom occurs in patients who receive prophylactic antitoxin after the trauma, and furthermore it is uncommon for tetanus to appear in such cases after a brief period of incubation. In Denmark during the decade 1932—41 a total of 16 instances of tetanus were observed in patients who had received prophylactic serum. Of them only four had an incubation period of less than 12 days (5).

*Clostridium tetani* is affected by penicillin. Penicillin treatment is ordinarily recommended for contaminated wounds, *int. al.* as a prophylaxis against anaerobic infections. Penicillin does not destroy tetanus toxin and penicillin does not have a convincing effect on a manifest tetanus (LEWIS 1946).

At the Rudolph Bergh Hospital in Copenhagen prophylactic tetanus antitoxin (3,000 A. U.) is given immediately to all contaminated burns and to all major burns. In addition, tetanus vaccine (toxoid) is administered in all cases likely to require subsequent transplantation. The injection of the vaccine is repeated on the 14th and 28th day. Moreover, all patients exhibiting contaminated burns or major burns are treated with

penicillin, 100,000 units 3 times daily. The reason why this prophylactic vaccine treatment is given in spite of the rare occurrence of tetanus following burns is that in 1947 a patient (a child) was lost from tetanus in connection with transplantation performed about 1 month after a severe burn. The patient had received tetanus serum on admission. (ASBO HANSEN.)

### Case Report.

Male, aged 25. Hospitalized on May 25, 1948. Burning alcohol had set fire on his clothes, and he rolled on the ground in order to put it out. Hereby he acquired burns of the third degree of the main part of both lower limbs and most of the right upper limb. Hospitalized immediately and treated with compressing bandages over sulfonamide ointment. On admission tetanus antitoxin, 3,000 A. U., was administered subcutaneously and tetanus toxoid, 1 ccm. also subcutaneously, but in two different injections. From the first day to the last he received penicillin, 100,000 units every 8 hours.

As regards the burn itself, the course was normal and the prognosis would presumably have been favourable, if tetanus had not supervened.

Exactly 10 days after the accident the patient complained of inability to open his mouth and rigidity of the neck. He was immediately given serum, 10,000 units subcutaneously and tetanus toxoid, 1 ccm. During the following night he was restless, sweated profusely and could only swallow drop by drop. Twenty-four hours after the onset of the trismus he was only able to open his mouth up to 1 cm. between the front teeth and exhibited rigidity of the abdominal muscles. Intramuscular administration of serum, 20,000 units, intramuscular magnesium sulfate, 20 per cent., as required, and an ordinary quiet regimen. Nevertheless, a typical attack of generalized tetanus supervened exactly 48 hours after the first symptom of tetanus.

In spite of ample magnesium sulfate, barbifen, and morphine the convulsions grew steadily more frequent, and about once every hour there was an attack of generalized reflex spasms attended with marked dyspnea and cyanosis.

We realized that the case would be hopeless treated by the ordinary measures and therefore asked Dr. E. Trier Mørch, the anaesthetist, to institute treatment with curare. This phase of the treatment will be reported by him in a separate paper.

In spite of all efforts the patient died 4 days after the onset of tetanus. Autopsy showed severe hyperemia in the lungs, edema and atelectasis, particularly in the upper lobes. Other pathologic changes were not found in the organs. Toxigenic *Cl. tetani* were not demonstrable on examination of some pieces of the burnt skin (The State Serum Institute).

### Discussion.

The case is an interesting and instructive one, revealing the following facts:

1) Although tetanus is of uncommon occurrence following burns, it is, however, a complication which must be borne in mind.

2) The protective effect of tetanus antitoxin (serum) is good, but not unfailing. As a rule the protection only lasts for about a week, a fact which has been dealt with in earlier papers (BRUCE, PERDRUP).

3) Active immunization (toxoid) does not afford any protection during the first fortnight following the injection, unless the patient has previously obtained active immunity.

4) Penicillin treatment of the infected wound does not afford a reliable protection against lockjaw, even when instituted immediately after the accident and continued during the entire period of incubation.

It is true that penicillin does affect the *Cl. tetani*, but apparently it does not reach the necrotic areas where the bacilli reproduce and produce toxin. The toxin, on the other hand, oozes through the barrier of granulations, and as it does not respond to penicillin, it can exert its toxic influence on the nervous system.

In view of the fact that treatment with curare involves a certain risk, it is important to be able to evaluate the intensity of the tetanus in each particular case. Of course an experienced clinician is capable of estimating the severity of the case by the violence of the symptoms. Still, each observer will only have the opportunity to see a few cases, and therefore the effect of future treatments, including the one with curare, can only be evaluated, if each worker describes the intensity of his cases by means of relevant, comparable and preferably numerical criteria.

Therefore the writer will refer to a Danish material of 527 cases of tetanus, the majority of which are derived from the decade 1932—1941, all of which occurred during peacetime, and in which the tetanus was treated in the usual manner with serum, magnesium sulfate, chloral hydrate — a few with avertin — and various other ordinary hypnotics. Hitherto this material has only been published in Danish (5).

Working with this material the writer succeeded in demonstrating two factors, both relevant, numerical and therefore comparable criteria of the intensity of the disease.

One is the period of incubation. The period of incubation means the time elapsing from the accident until the first symptom of tetanus. Table 1 shows the relation between period of incubation and lethality.

Table 1.

*Number of Patients and Lethality in Relation to the Various Periods of Incubation.*

(Not including patients who had received prophylactic serum.)

Period of incubation, days	Number of patients	Deaths	Lethality %
3.....	5	1	20
4.....	7	6	85.8
5.....	12	11	91.8
6.....	28	16	57.1
7.....	32	19	59.5
8.....	51	21	41.2
9.....	23	11	47.8
10.....	33	8	24.2
11.....	18	4	22.2
12.....	28	8	28.6
13.....	15	4	26.6
14.....	32	5	15.6
15.....	5	1	20.0
16.....	3	0	
17.....	3	0	
18.....	1	1	
19.....	1	0	16.7
20.....	5	0	
21.....	20	5	
> 21.....	4	0	
unknown .....	175	63	36.0
< 8.....	3	2	
< 10.....	1	1	
> 10.....	3	1	
> 14.....	1	0	
Total.....	509	188	37.0

A more perspicuous view of the relation between lethality and period of incubation is afforded by Diagram 1.

The other factor is the so-called period of onset, originally defined by COLE as expressing the rate at which the disease passes from one stage to another. According to COLE's definition the period of onset means the time elapsing from the first symptom of tetanus until the first reflex spasm is observed, *i. e.* between two easily recognizable symptoms. Table 2 sets out the relation between the period of onset (measured in 24-hour periods) and

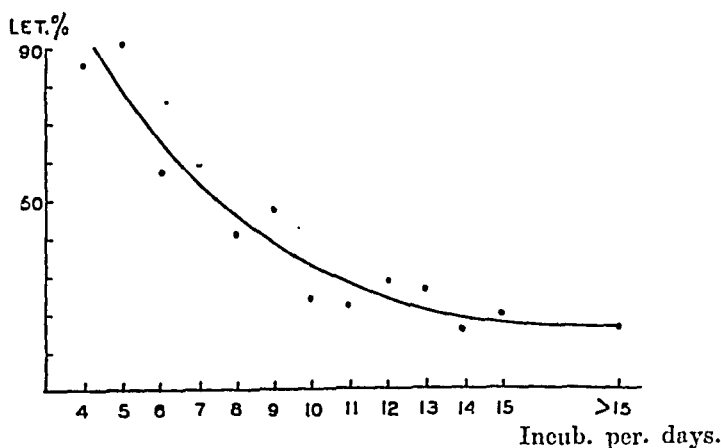


Diagram 1.

Graphic representation of Table 1.

the lethality. A period of onset of  $\infty$  means that reflex spasms have not been observed or reported in the original case reports.

Table 2.

*Number of Patients and Lethality in Relation to the Various Periods of Onset.*

Period of onset, in 24-hours	Number of patients	Deaths	Lethality %
ab. ] 0.25.....	12	9	75
» 0.50.....	11	10	91
» 0.75.....	5	5	100
» 1.0.....	29	24	82.7
» 1.5.....	19	13	68.3
» 2.0.....	33	17	51.5
» 2.5.....	31	14	45.2
» 3.0.....	27	10	37.1
» 3.5.....	7	2	28.6
» 4.....	50	17	34.0
» 5.....	23	6	26.1
» 6.....	24	7	29.2
» 7.....	9	1	11.1
» 8.....	13	1	7.7
» 9.....	1	0	—
» 10.....	10	0	0.0
» 14.....	1	0	—
< 2.....	4	3	
> 2.....	2	1	
< 3.....	2	2	
> 3.....	7	0	
$\infty$ .....	177	39	22.0
unknown.....	30	16	53.4
Total.....	527	197	

For the sake of perspicuity a graphic representation of Table 2 is given in Diagram 2.

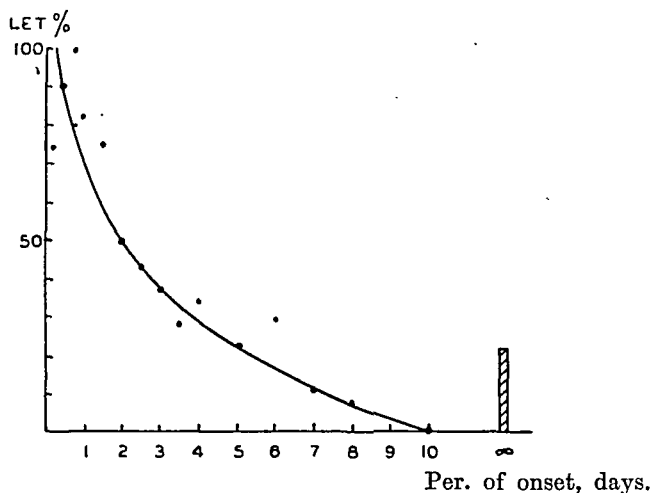


Diagram 2.

Relation between Period of Onset and Lethality. (Graphic representation of Table 2.)

Next it was investigated whether it might be possible to find a numerical collective term for period of incubation and period of onset, as there ought to be a distinct relationship between it and the course of the disease. Seeing that period of incubation and period of onset are two consecutive phases of the disease and that the lethality has proved to decline upon increase in both phases, it would appear natural that the sum total of these two periods was suitable for this end.

However, empirically the product of the period of incubation and the period of onset proved to be more practical.

Table 3 sets out the distribution of the material with regard to the product  $I \cdot O^1$  as well as the lethality in relation to the different values of this product.

Table 3.

Product of period of incubation and period of onset. $I \cdot O$	Number of patients	Deaths	Lethality %
0— 5.....	23	21	91.4
6— 10.....	20	15	75.0
11— 20.....	35	24	68.6
21— 30.....	32	13	40.6
31— 40.....	22	8	36.4
41— 50.....	17	4	23.5
51—100.....	26	2	7.7
> 100.....	11	0	0.0
Total .....	186	87	46.7

<sup>1</sup> I = period of incubation.

O = period of onset.

From Table 3 and Diagram 3 it will be seen how the lethality falls from about 90 per cent at an  $I \cdot O$  of 0—5 to 0 at an  $I \cdot O > 50$ .

In cases where both period of incubation and period of onset are known, the product  $I \cdot O$  appears to be a good expression of the prognosis and consequently also of the intensity of the disease. Patients with a period of onset =  $\infty$  are not included in this calculation.

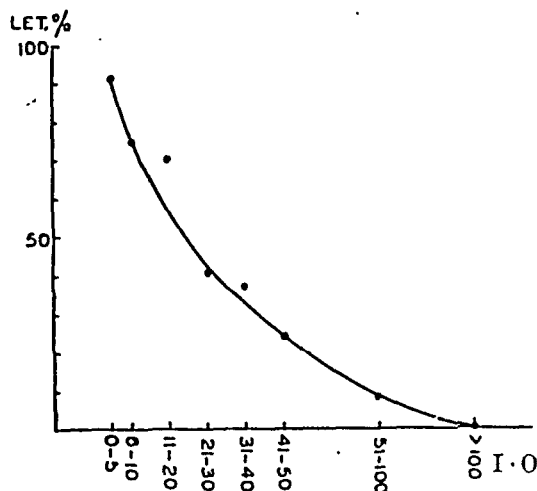


Diagram 3.

Graphic Representation of Table 3 Showing the Relation Between the Product  $I \cdot O$  and the Various Percentages of Lethality. (Not including the patients who had received prophylactic serum.)

In the case under discussion the period of incubation was 10 days and the period of onset 2 days. According to Table 3 and Diagram 3  $I \cdot O = 20$  indicates a rather serious prognosis.

If all workers reporting the results of treatment of tetanus would state the period of incubation and period of onset, it would be possible to obtain valuable collected statistics and to arrive at a rational evaluation of the effect of new forms of treatment. In the absence of comparable criteria of the intensity of the disease, a real evaluation of the effect of new methods of treatment is practically impossible.

### Summary.

A report is given of a fatal case of tetanus following burns. On the day of the accident the patient had received both serum and vaccine, and the burns were treated with penicillin from the first day. The effect of the prophylactic measures is discussed.



The period of incubation and the period of onset are dealt with as relevant, comparable, numerical criteria of the intensity of the disease.

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From the State Hospital, Copenhagen: Out Patient Surgical Service  
(Chief: Professor ERIK HUSFELDT, M. D.) and Department of  
Radiology (Chief: Professor FLEMMING MØLLER, M. D.)

## Lunatomalacia.<sup>1</sup>

By

FREDERIK THERKELSEN and KJELD ANDERSEN.

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The interest which still attaches to lunatomalacia (Kienböck's disease) is mainly due to two reasons. In the first place its pathogenesis still presents many problems in spite of the great efforts made in the course of time to throw a light upon its mysteries, and in the second place there does not yet exist a treatment which can be said to affect the disease favorably with a fair amount of certainty.

Before proceeding to report their own investigations the writers will briefly review the theories advanced about the pathogenesis of this disease as well as earlier investigations into its morbid anatomy and treatment.

### *Pathogenesis:*

Lunatomalacia is often classified with the group of aseptic bone necroses (AXHAUSEN), because it is one of a number of localized, aseptic bone diseases which possess certain common clinical and roentgenologic signs. It must, however, be admitted — prior to further pathogenetic contemplations — that lunatomalacia at any rate occupies an exceptional position (JAROSCHY, SCHNEIDER, ØSTERGAARD-CHRISTENSEN), if it does belong to the group at all, as it is most commonly met with after bone growth is completed, unlike all other types of aseptic bone necrosis. In

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<sup>1</sup> The part on the pathogenesis was read, in an abbreviated form, before the meeting of the Danish Orthopedic Society on January 16, 1948 — and the part on prognosis and treatment, also in an abbreviated form, before the meeting of the Danish Society of Surgeons on March 13, 1948.

addition, other types exhibit a marked tendency to spontaneous healing which is comparatively rare in lunatomalacia.

Briefly, the main theories are as follows:

1) KIENBÖCK is of opinion that a contusion or distortion involving impairment of ligaments and thereby also interference with the blood supply results in necrosis of the bone giving the characteristic picture.

2) MÜLLER maintains that because of its exposed position below the radial articular surface, the semilunar — due to frequent traumas — becomes the seat of a hitherto unknown morbid process which gradually develops into the well-known picture of lunatomalacia.

3) According to AXHAUSEN it is a question of necrosis resulting from embolic processes.

4) HIRSCH explains the conditions as a result of a fracture caused by a single trauma. The subsequent characteristic course should then be due to the formation of a false joint (KAPPIS).

Although the theory of fracture has many supporters (DESTOR, KONJETZNY, CORDES, H. MØLLER, J. JENSEN) we still lack the demonstration of a pure fracture developing into lunatomalacia. FABRICIUS-MØLLER who in his paper from 1919 considered the reason to be a primary fracture, has now abandoned this view. According to SCHINZ, BAENSCH & FRIEDL's textbook the disease is interpretable as a pathologic compression fracture resulting from a bone necrosis of unknown etiology, and it is added that if trauma is of any significance it must be a case of chronic traumas sustained in the course of a long time.

STÄHL, however, reports that he has demonstrated unquestionable compression fracture (otherwise normal bone) in 4 cases.

5) A certain constitutional factor would appear likely in view of the not uncommon occurrence of bilateral involvement. RINGSTED's cases of bilateral lunate malacia in two brothers would indicate a hereditary predisposition.

6) Among other presumed causes there are streptococci (PHEMISTER, BRAUNSCHWEIG & DAY) as well as vitamin and hormone insufficiency (SCHNEIDER).

By now it is on the whole generally agreed that KIENBÖCK's theory is untenable, *int. al.* because dislocation of the semilunar is not followed by malacia (JAROSCHY, WETTE, CORDES) except in extremely rare cases (CAVE has published one which he considers to be the only one reported). It is also considered to have been proved that AXHAUSEN's interpretation does not either explain the origin of the condition, as numerous anastomoses at any rate rule out major infarctions (*int. al.* KAPPIS). Moreover, it is quite incomprehensible that the semilunar should be the only carpal bone where an embolus should become impacted.

There is a growing tendency to interpret the disease as being

of traumatic origin, mainly because it has been recognized that the semilunar is particularly exposed to pressure in the direction of the long axis of the arm and that the condition is definitely most common in manual workers (especially in those working with pneumatic tools (ROSTOCK, WETTE, TILLMANN) of the most active age. The fact that the semilunar bone may in certain cases be particularly exposed has been shown by HULTÉN, investigating the relation between the position of the distal articular surfaces of the radius and ulna. He has found that in cases affected with lunatomalacia the radial joint surface is more frequently distal to that of the ulna than in normal subjects.<sup>1</sup>

The next question to be considered is whether the traumatic action causing the disease is a single trauma resulting in fracture of a healthy bone or whether it is a case of repeated traumas gradually producing a kind of brittleness of the bone and slow disintegration.

### *Pathology:*

The pathologic findings in lunatomalacia are of the utmost importance to the understanding of its pathogenesis. According to the studies reported so far, the changes found may be of traumatic origin, whereas nothing appears to indicate the presence of specific bone diseases (CORDES, HÜHNE, KONJETZNY).

### *Prognosis and Treatment:*

On the whole the prognosis is considered unfavorable (int. al. WEIL) and accordingly the methods of treatment are numerous.

### *Conservative Treatment:*

Originally cases in the early stages were treated with immobilization and in addition extension on the middle finger (FINSTERER, HIRSCH), but gradually the conservative treatment has been limited to plaster bandage for a varying length of time. This is probably still the most common method of treatment, especially in the early stages (JAROSCHY, HIRSCH, HONKANEN).

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<sup>1</sup> HULTÉN calls the cases in which the radial joint surface is more distal than the ulnar one "minus variants", those in which both surfaces are on the same level "zero variants", and those in which the ulnar joint surface is more distal "plus variants".

### *Operative Treatment.*

*Excision of the semilunar* is recommended by several workers (BAUM, JAROSCHY, KAPPIS, PARTSCH, BENTZON, FABRICIUS-MØLLER, RINGSTED, TARP). Most workers first try the conservative treatment; a few others, including FAUST, regard the condition to be completely refractory to conservative measures and therefore advise excision even in the early stages. BÖHLER — who also doubts the value of conservative treatment — advises definitely against operation.

Among other surgical procedures there are *excochleation of the semilunar bone* (WALLER, MÜLLER) sometimes followed by a filling of the resulting defect with plaster of Paris (NORDMANN) — *drilling of the lunate* (KONJETZNY) perhaps combined with introduction of a bony graft into the semilunar (SCHNEIDER) — *chiselling of the dorsal cortical plate* ("KONJETZNY's operation") which also is recommended by SCHIPPOREIT — and *operations upon the sympathetic nervous system* (LERICHE). It applies to all these methods that the numbers involved are too small and that sufficient follow-up work is lacking.

The main therapeutic measures are still immobilization in plaster of Paris and excision, and the investigations made so far seem insufficient to decide which method is the best one or whether any of them is at all capable of improving the results.

A method introduced during recent years is HULTÉN's *shortening of the radius* intended as a causal treatment reducing the pressure of the radial joint surface on the semilunar and thereby giving a greater chance of healing. Because of the drawbacks of shortening of the radius which does not seldom lead to a bending of the bone, PERSSON performs a prolongation of the ulna which, however, sometimes results in the formation of a false joint. The results appear to be promising, but as yet the number of cases is too small.

### Writers' Investigations.

The writers set themselves the task of:

1) Trying to contribute to throwing a light on the pathogenesis of the malacia<sup>1</sup> of the semilunar bone by means of a roentgenologic material.

<sup>1</sup> The term "malacia" is used throughout this paper. It is used as a collective term for all the roentgen changes in the lunatum belonging to this condition, even if they are represented more or less by fractures. It does not, however, include superficial chipping off of bone, if the bone otherwise looks perfectly normal.

2) Investigating the prognosis on the basis of follow-up studies compared with the roentgen findings.

The material is derived from the Out Patient Surgical Service and the Surgical Departments of the State Hospital as well as from the Orthopedic Hospital, Copenhagen, covering the 10-year period 1934—43. In addition, it includes a few cases from the material of the Directorate of Accident Insurance from the same period.<sup>1</sup> A few cases about whom details were lacking have been left out of account. Moreover, the material only comprises cases in which the roentgenograms were accessible or the roentgen report characteristic.

The material comprises 109 cases of malacia occurring in 107 patients, and the follow-up 92 cases among 90 patients. In 61 cases roentgenograms have been obtained, either in Copenhagen or from the provincial towns. The follow-up was conducted by the writers personally, although a certain number of patients from distant parts of the country only sent replies to questionnaires.

*Pathogenesis:* When the material is regarded as a whole, it strikes one at once that the great majority of the patients are *manual workers* (98 of 107). This might of course be attributed to the possibility that the Out Patient Service were mainly attended by manual workers. Still, STÅHL, who like many others found a perceptible predominance of manual workers in his material of malacia has demonstrated that while 97 per cent. of these patients had manual work only 85 per cent. of all the patients attending the Orthopedic Clinic in Lund, Sweden, were engaged in manual work. Such a calculation could not be made in our material, as it is derived from different places.

Only 26 of the patients of our material were females and only 31 of the cases were left-sided.

There was a history of a fairly unquestionable *trauma* in 42 cases (38 per cent.), a comparatively large percentage in relation to other materials. By way of comparison it may be stated that in a corresponding material of fractures of the carpal scaphoid — which we also studied — there was a history of definite trauma in 118 of 120 cases (98 per cent). In the latter material it was also as a rule a question of more severe traumas.

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<sup>1</sup> To the Chief Surgeons of the Departments of Surgery, State Hospital and of the Orthopedic Hospital as well as the Directorate of Accident Insurance our thanks are due for permission to work with the material.

A further study of the radiograms available reveals the following:

Like HULTÉN and PERSSON we have divided the cases according to level differences. (Table 5 b. 1st column.)

This revealed more minus variants (42 per cent) than in a normal material (*e. g.* JOECK had 9.4 % in his normal material but 63.9 % in his material of Kienböck's malacia). HULTÉN has 17 minus variants (73.8 %) among 23 cases.

In cases of zero and plus variants the *change in shape* presents itself in the form of a rather uniform decrease in height of the entire bone with a considerable increase in breadth in the antero-posterior view. In cases of minus variants, on the other hand, the lowest part of the semilunar is usually the one covered by the radius. Accordingly, the nature of the deformity of the lunatum will in most cases be sufficient to decide whether it is a question of a minus, zero or plus variant (See Figs. 1, 2, 3). The increase in breadth is nearly the same in the various types.

The *structural changes* afford an extremely motley picture, even in the first roentgenograms. There are variations from thin, condensed lines resembling the sequels of compression fractures in a slightly patchy bone to marked changes with major or minor areas of translucency and others of density, as if the bone had broken into numerous fragments (Fig. 3 and 9). In other cases the structure is of a peculiar, irregular, "shaggy", vacuolized appearance (Fig. 12 a). Moreover, there may be a marked horizontal stratification.

In addition to the structure resembling compression fracture there may often be vertical fractures which usually are of an antero-posterior course (Fig. 6).

The *only constant* phenomenon is, however, the usually extremely marked flattening of almost the entire bone. This flattening is always most conspicuous in the lateral view.

As to the *extent* of the structural changes this varies, particularly in the first roentgenograms. It appears, however, that in the zero variants (and plus variants) the changes usually apply to the entire bone, whereas minus variants are mostly restricted to the part covered by the radius.

A question of the utmost importance with regard to pathogenesis is the *appearance of the first roentgen signs* of the disease and its further *course*.

It is difficult to throw a light upon this question because of

## LUNATOMALACIA.

the frequently insidious course without any definite trauma. Therefore the first roentgenograms are not as a rule taken until months or even years after the disease must be presumed to have set in. And in case there has been a trauma, neither the trauma itself nor the subsequent symptoms are severe enough to send the patient to a physician.

The mildest changes we have found which perhaps are interpretable as the initial stage, consisted of a faint increase in density — apart from the decrease in height. Five cases (Figs. 1, 2, 3, 4, and 5) presented a picture which *at first glance might have been taken for compression fracture*. On closer inspection it appeared, however, that apart from the fracture lines there were small areas of density in major or minor parts of the remaining bone. One of the cases (Fig. 3) is exceptional in showing the increased density exclusively localized below the distal joint surface — and the flattening of the bone only amounts to fractions of a millimeter. The proximal joint surface is slightly wavy (the roentgenogram made 1 year after onset of symptoms). In the above-mentioned 5 cases the roentgenograms were obtained 3 months, 6 months, 1 year and 2½ years after the presumed onset of the disease. Only in 1 case (56) trauma was stated to have elicited the symptoms.

*A picture resembling a compression fracture may thus be encountered in cases of extremely varying duration.*

The material only contains 2 cases radiographed immediately (1st day and 1st week respectively) *after a definite trauma* (see Figs. 6 and 7). In addition to the flattening the first case exhibits scattered areas of density and a vertical frontal fracture, but no sign of compression fracture. According to most workers such vertical fractures are only met with in long-standing cases. In the other case there were roentgen signs of an advanced malacia.

















These 7 cases clearly show how apparently irregular are the roentgen signs at the various stages of the disease and how careful one must be in interpreting a picture resembling a compression fracture as a fresh injury. The cases dealt with above are set out in Table 1.

In the remaining cases the first roentgenograms show typical malacias at a more or less advanced stage, definitely not interpretable as compression fractures in healthy bone.

A study of the roentgenologic course reveals that it is impos-



Table 1.

Case:	Age:	Trauma:	1st roentgenogr. after:	1st <u>roentgenogr.</u>	Last roentgenogr. after:	Last <u>roentgenogr.</u>
1 (carpenter)	33	÷	1 year		6 years	
21 (carpenter)	36	÷	3 months		5 years	 (healing)
47 (railway parcel sorter)	56	÷	8 years		12 years	
56 (housemaid)	16	+	2 1/2 years		12 years	 (healing)
109 (farmer)	21	÷	(2 months) 6 months		8 years	
17 (laborer)	57	+	1 day	 	(5 years)	  (Roentgen appearance 1 yr. later whereupon excision)
78 (farmer)	26	+	1 week		8 years	

sible to demonstrate well-defined stages in the development. This diversity in the nature of the roentgenologic aspect may partly be due to factors like level differences and different ages. As to the significance of the latter, the writers have gained the impression that in young subjects it seems as if the lunatum is squeezed out like a plastic body (Fig. 10), whereas in subjects of a more advanced age fragmentation will occur.

By following the cases up for a number of years it appears to be possible to decide with certainty whether *healing* occurs.

Among the 61 cases followed up by roentgen ray the process has undoubtedly healed in 9 (see Table 2). The criterion is that the bone structure has become uniform and shows a normal pattern and the same density as the other carpal bones. The shape, on the other hand, remains abnormal, except in one case (Fig. 8).

Table 2.  
9 Healed Cases.

No.	Age at 1st symp-tom.	Occupation	Trauma	Period from 1st symptom to roent-genogr.	Treatment after diagn. has been made <sup>1</sup>	Period from 1st sympt. to last roent-genogr.	Functional result.
11	11	Son of glass-blower	+	6 months	Plaster bandage 3 months.	5 years	Ideal.
73	15	Farmer	÷	6 months	Plaster bandage 13 months	2 years	Poor.
56	16	Housemaid	+	2½ years	Plaster splint 6 months	12 years	Ideal
7	18	Farm-hand	÷	4 months	Plaster bandage 4 weeks. Elastoplast	6 years	Good
16	18	Country house-wife	÷	?	Plaster bandage more than 1 year	4 years	Poor
39	19	—	+	1 year	Plaster splint 3 weeks	12 years	Ideal
57	20	Herdsmen	÷	9 months	Plaster bandage 8 months	3 years	Good
88	21	Farmer	÷	2 months	Plaster bandage about 1 year	7 years	Ideal
21	36	Carpenter	÷	3 months	Plaster bandage 5 months	5 years	Ideal

This patient had acquired the disease at the age of 11, and normal structure and shape were regained in 3 years. In this case it cannot, however, be ruled out entirely that it was a question of actual fracture (and not malacia), as the roentgenogram rather suggests it (shelly division of the bone) and the trauma was a severe one (patient was run over).

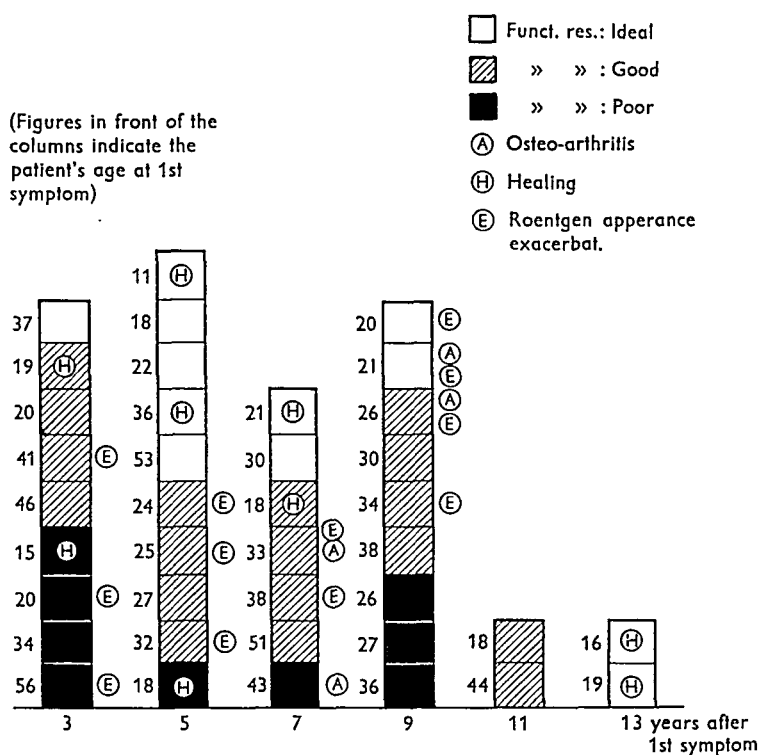
It would appear that healing preferably occurs in cases acquired at an early age. This may, however, be mainly due to the fact that young people make up the majority of the material (see Table 6).

Table 3, setting out all *non-operated cases* according to duration of the disease (from first symptom to follow-up), shows that the earliest healings occur within the first 3 years (in one case healing

<sup>1</sup> Before the diagnosis is made the patients are usually treated with massage, heat, bandage etc.

Table 3.

*39 Cases Re-examined with Respect to Functional and Roentgenologic Result (not including cases submitted to excision of the semilunar).*



was observed in 2 years). The remaining healed cases are distributed over the following 10 years. It will be seen, however, that even up to 9—11 years after the onset several cases show no signs of healing and in a total of 12 cases the process must be characterized as having been exacerbated, *i. e.* there are more areas of rarefaction and fragments and simultaneously the flattening increases.

#### *Other Changes in the Wrist:*

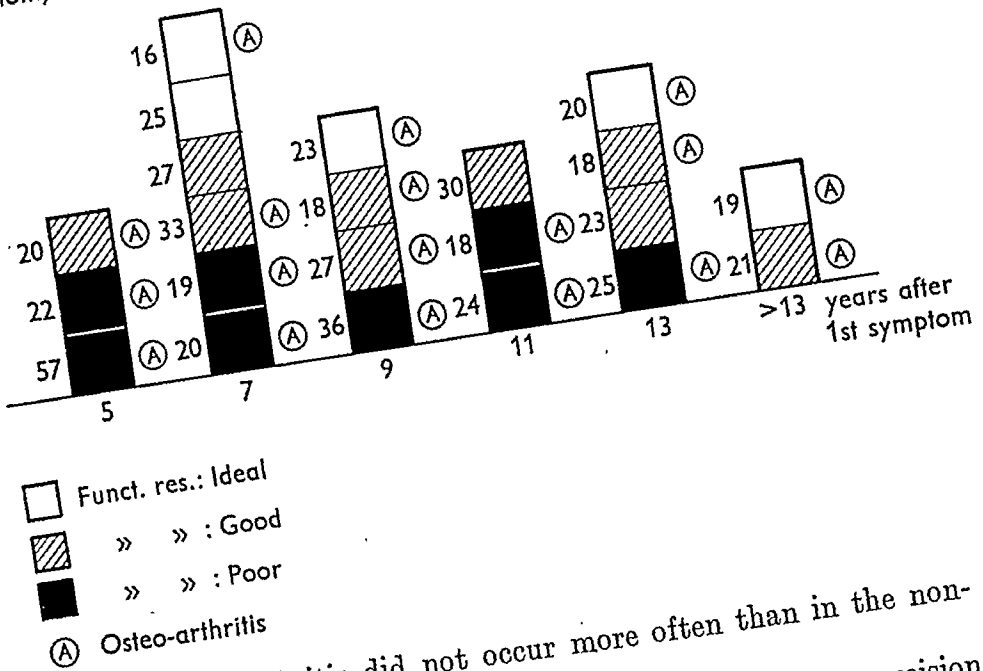
1) *Osteo-arthritis*, definitely demonstrable by roentgen ray, was observed in 23 of the 61 cases. It is, however, far more common in cases submitted to excision (19 out of 22 cases, see Table 4) than those not operated upon (4 out of 39). It should be mentioned here that among the cases radiographed prior to the ex-

## LUNATOMALACIA.

Table 4.

22 Cases Submitted to Excision of the Semilunar Bone  
Re-examined with Respect to Functional and Roentgenologic Result.

(Figures in front of the columns indicate the patient's age at 1st symptom)



cision osteo-arthritis did not occur more often than in the non-operated cases.

2) In cases of marked flattening of the semilunar or excision of the bone, there is often a more or less marked subluxation of the scaphoid (Fig. 11).

3) In a few cases changes were observed in the adjoining bones. One of these will be reported briefly below:

Case 22: A female, aged 23, who had not exhibited changes in other carpal bones before the excision of the semilunar. As early as 6 months after the operation changes were observed in the scaphoid and at the follow-up 6 years later there was marked subluxation of the scaphoid which was pressed in below the joint surface of the radius. Corresponding to the presumed pressure, the pattern was condensed and sclerosed. Moreover, there appears to be a fracture line approximately through the middle of the bone where the increased density meets the more normal part of the bone. The distance from the radius to the os magnum is decreased from 13—9 mm. Some osteo-arthritis (functional result: ideal). (Fig. 12.)

Such structural changes arising after the pressure in the wrist has shifted to other bones — because of the flattening of the semilunar or its removal — are presumably interpretable as a reaction to alteration in pressure. A comparison can be made with the sclerosing which often arises in the upper part of the acetabulum in consequence of "incongruity" in the hip joint.

It would be reasonable to presume the existence of a condition resembling malacia arising in this way in the carpal bones in question, but the present investigations do not furnish the proof.

Similar changes in the neighbouring bones in cases of malacia do not appear to have been described earlier. Still, KIENBÖCK reported that he had observed superficial porosis of the styloid processes of the ulna and radius in a case of chronic arthritis of the wrist combined with malacia of the os lunatum.

According to the observations made we regard *the pathogenetic interpretation* of malacia which attributes *repeated traumas with a predominant significance* to its onset and development to be the most probable one.

The findings, earlier ones as well as the writers', which support this interpretation may be *summarized* as follows:

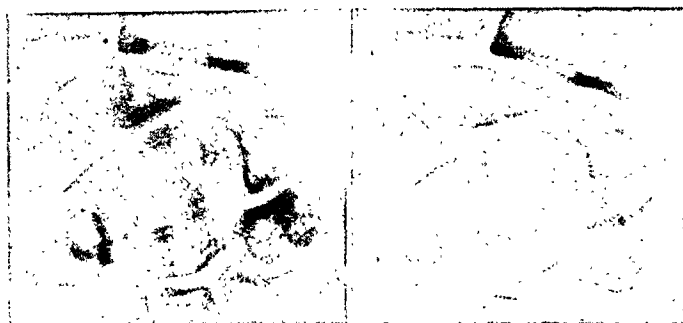
- 1) That the effect of pressure is a matter of great significance to the onset and development of the lesion, is strongly suggested by investigations into level differences and the demonstration of the fact that deformity and structural changes are quite particularly localized to those parts of the bone where the pressure must be presumed to be most heavy. The great predominance among manual workers and the vast majority of cases involving the right side point in the same direction.

- 2) The writers' observation of radiological changes in neighbouring bones in a few cases where the semilunar is greatly flattened or has been removed demonstrates the significance of pressure on the bones which are most exposed after the semilunar.

- 3) Pathologic findings made so far do not contradict a purely traumatic genesis.

- 4) GÖCKE's experiment (on the cadaver) on the effect of repeated traumas or injuries with protracted consequences on spongy tissue support the theory of repeated traumas.

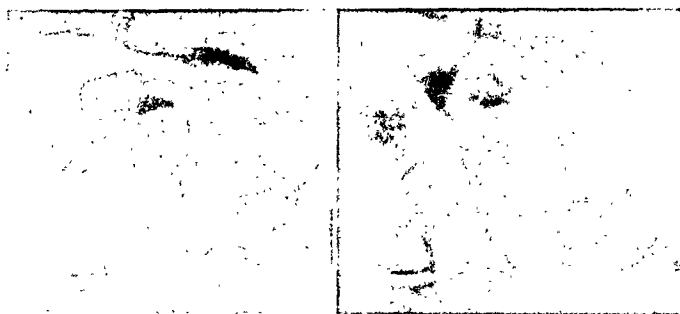
- 5) In other parts of the skeletal system one may meet with changes which — even if they in other respects differ from those



a.

b.

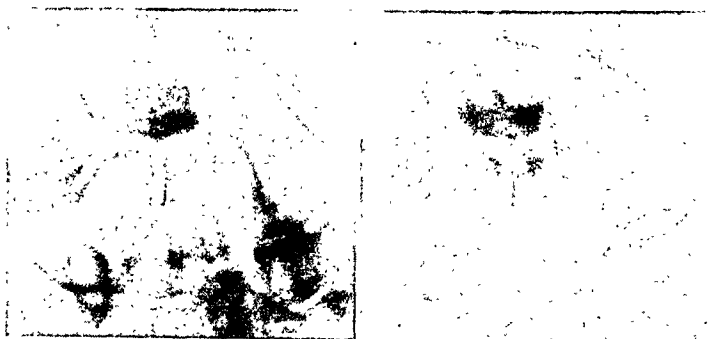
Fig. 1. Case 21. Male, aged 36, minus variant. 3—4 months prior to roentgenography (a) he had been aware of a reduced power in his right hand. Changes resembling compression fracture in the radial part of the semilunar bone. (b) healing 5 years later.



a.

b.

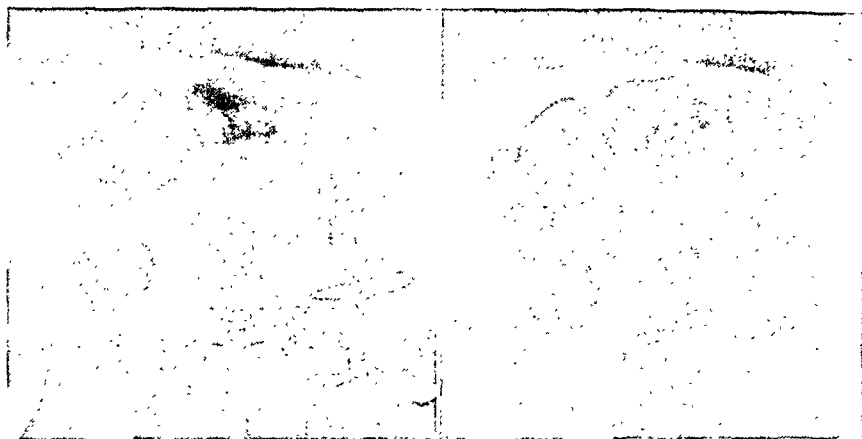
Fig. 2. Case 109. Male, aged 21, minus variant. Insidious onset 2 months prior to roentgenography (the reproduced fig. (a) is, however, taken 4 months later, after plaster bandage had resulted in haliteresis). The structure resembles compression fracture in the radial part. 8 years later (b) extensive changes in the entire bone.



a.

b.

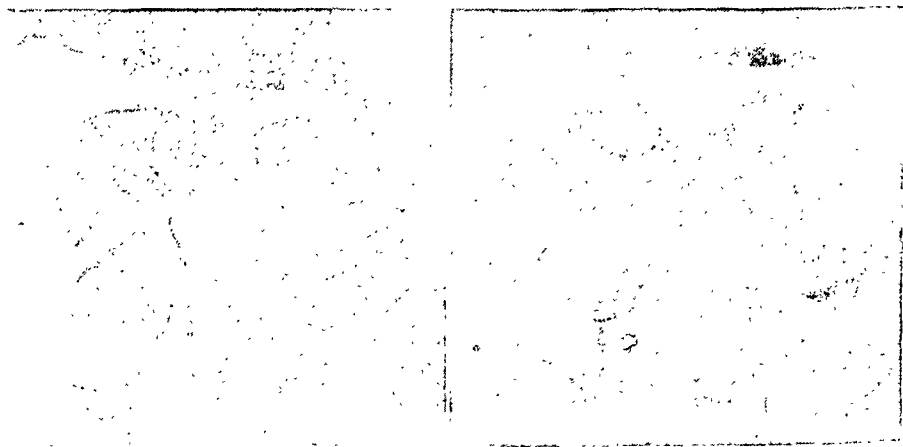
Fig. 3. Case 1. Male, aged 33, zero variant. (a): First roentgenogram taken 1 year after onset of symptoms. No history of trauma. (b): Roentgenogram 6 years later shows a considerably advanced process. Only slight flattening.



a.

b.

Fig. 4. Case 56. Female, aged 16, zero variant. (a): Roentgenogram taken  $2\frac{1}{2}$  years after a definite trauma. Structure resembles compression fracture through almost the entire bone. (b)  $9\frac{1}{2}$  years later. The process has healed.



a.

b.

Fig. 5. Case 47. Male, aged 56, zero variant. (a): Marked flattening on the radial aspect where the structure resembles compression fracture. Taken 8 years after first symptom. No history of trauma. (b): 4 years later. Advancing process.

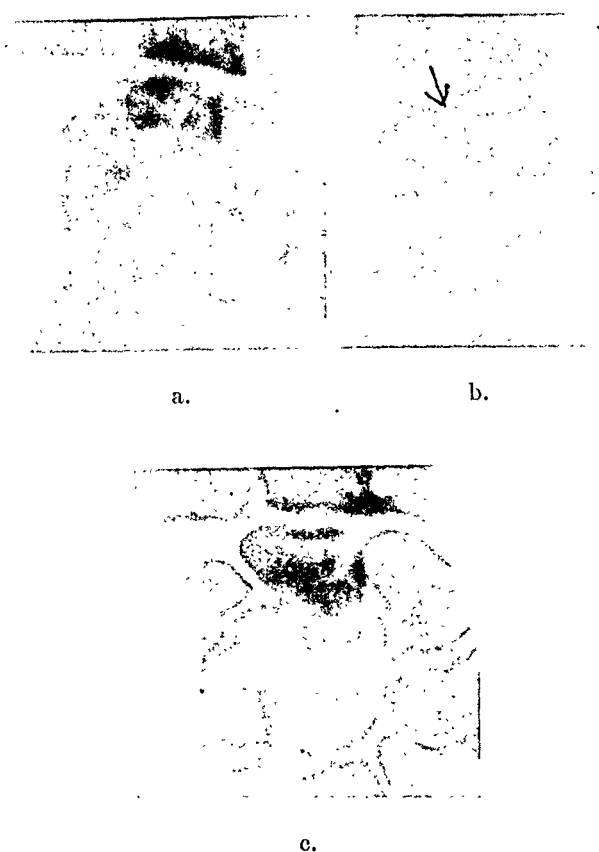


Fig. 6. Case 17. Male, aged 57, zero variant. First roentgenograms (a—b) taken *the day* after a definite trauma. Patient has been perfectly symptomless before. Lateral view reveals a distinct, frontal, vertical fracture. Pathologic changes in the remaining part of the bone. (c): 1 year later the process has advanced.

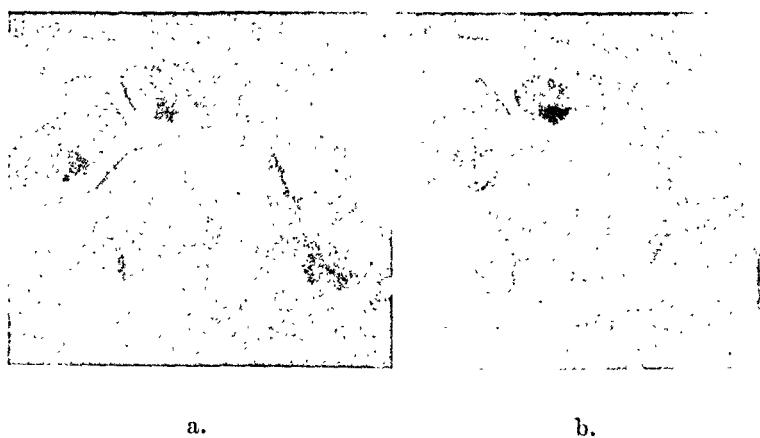
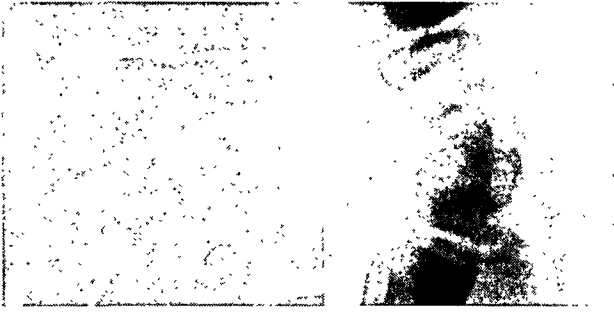


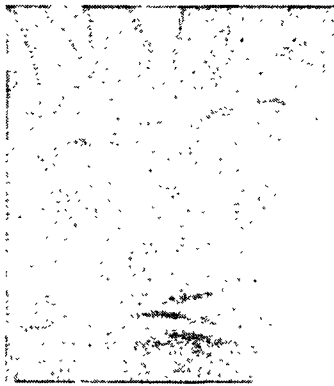
Fig. 7. Case 78. Male, aged 20, zero variant. (a) Roentgenogram taken 1 *week* after a definite trauma, shows typical, marked, advanced malacia. (b): 8 years later exacerbation of the process.





a.

b.



c.



d.

e.

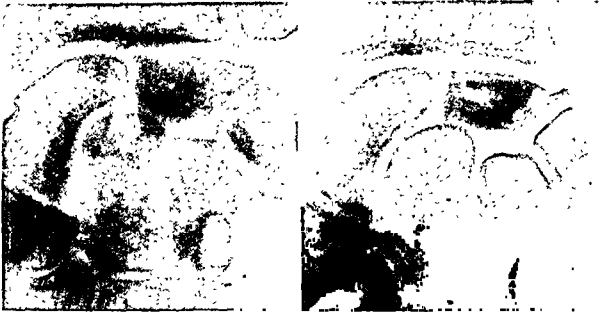
Fig. 8. Case 11. Boy, aged 11, minus variant (a—b). 6 months after being run over he exhibits perceptible flattening of the semilunar bone. ((c—d) the unaffected wrist for comparison.) 5 years later healing (e). Between the semilunar and scaphoid there is a small shadow, presumably representing a shelly fragment which has not healed.



a.

b.

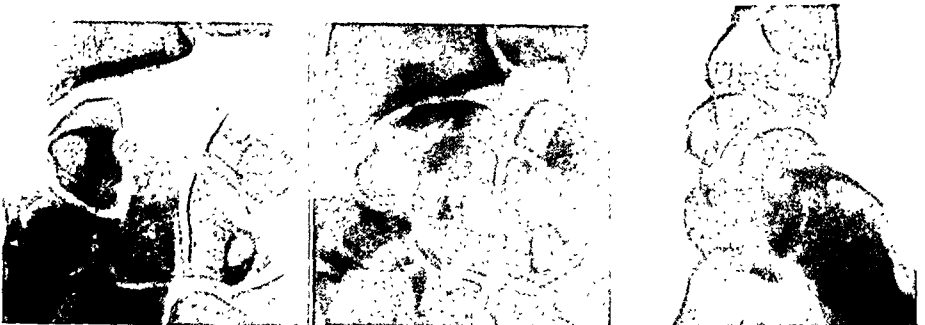
Fig. 9. Case 100. Male, aged 30, minus variant. Insidious onset 3—4 months before 1st roentgenogram. (a) Marked deformity of semilunar bone which exhibits fracture lines. (b): 1 year later the process has advanced further.



a.

b.

Fig. 10. Case 57. Male, aged 20, minus variant. No history of trauma. During the last year prior to roentgenography (a) dorsal flexion of the left wrist had been impossible. Marked changes in the semilunar with plastic lengthening towards the ulnar side. (b): healing 2 yrs later.



a.

b.

c.

Fig. 11. Case 65. Female, aged 20, minus variant. (a) Excision of semilunar bone. (b—c): 6 years later there is subluxation of the scaphoid.

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a.

b.



c.

d.

Fig. 12. Case 22. Female, aged 23, zero variant. Prior to the excision of the sesamoid there had been no changes in the scaphoid (a), which 6 months later exhibits increased density (b), and 6 years later (c) marked changes and fracture. In addition, increased density in the proximal part of the os magnum (d: lateral view).

of malacia — are considered by many workers to arise from repeated traumas. One need only remember march fracture and changes in the tibia which are characterized by Looser's transformation zones.

As regards the question of a *single trauma* supposed to cause a fracture in an otherwise normal bone, the writers are of opinion that although STÅHL's investigations rather point into this direction, this mode of origin is at any rate extremely rare, because: 1) There is seldom a definite history of a single trauma and 2) the various roentgenologic types do not appear to follow any rules. The few cases of our material resembling compression fractures also exhibit areas of density in the remaining bone and are observed in cases of very different duration. In addition, the only two cases radiographed immediately after an undoubted trauma — cases which were perfectly symptomless before — presented a picture which could only be interpreted as long-standing malacia.

The comparative frequency of bilateral involvement and the occasional observations of familial occurrence do not affect the traumatic theory, as it is by no means unlikely that a, perhaps genetically ruled, brittleness of bones may be a contributory factor.

### *Prognosis and Treatment:*

In the present material the period of observation (from the first symptom) is 3—14 years (average 6.6 years).

An *ideal* result means: No discomfort of any kind. Objectively normal conditions.

» *good* » : Mild discomfort, constantly or intermittently, or objective changes. Working ability in usual occupation unchanged.

» *poor* » : Severe discomfort involving reduced working ability, perhaps a change of occupation.

Tables 5 and 6 set out the result of the follow-up. In Table 5 b the 79 radiographed cases are grouped according to level differences. The prognosis appears to be best in the zero variants.

Table 5.

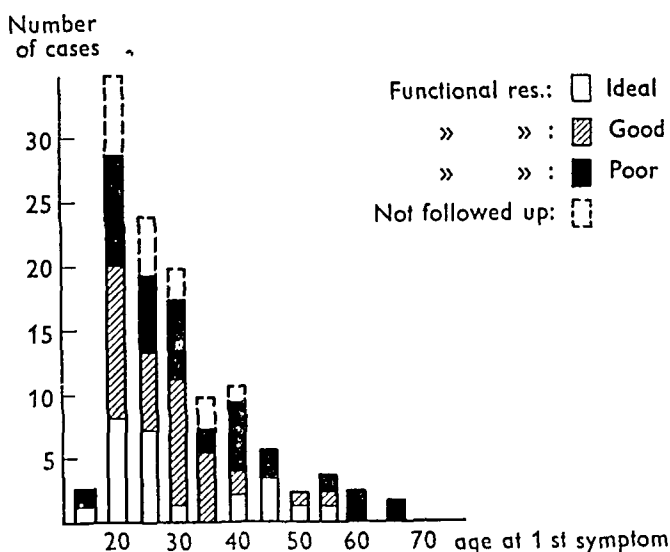
*a: Functional Result in Entire Follow-up Material.*

Number	Ideal	Good	Poor
92	21	40	31

*b: Roentgenographed Cases Classified According to Level Differences.*

	Number	Not followed up	Cases followed up		
			Ideal	Good	Poor
Zero variants .....	44	6	5	25	8
Minus variants .....	33	3	6	11	13
Plus variants .....	2	1		1	
Total	79	10	11	37	21

Table 6.

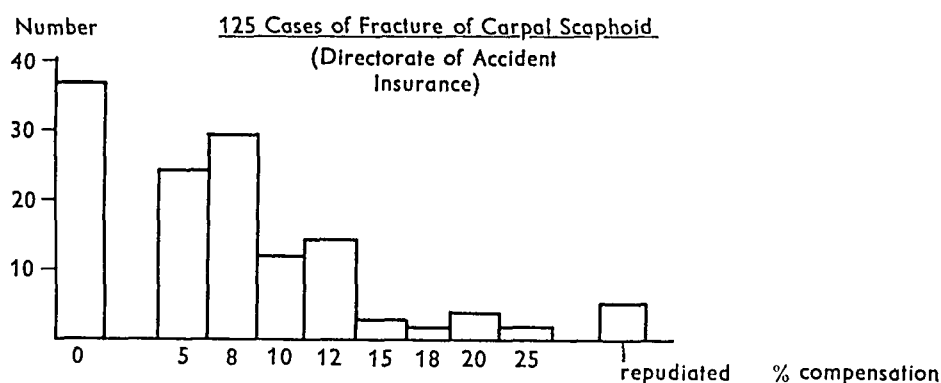
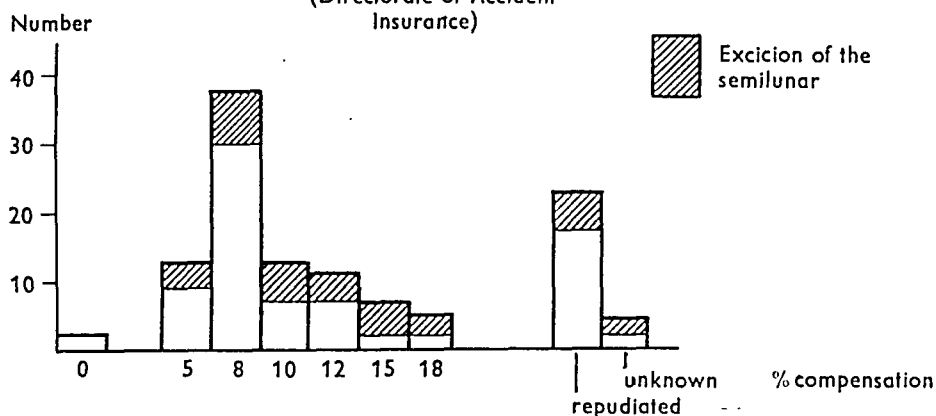
*Total Number of Cases (109) Set Out According to Functional Result and Age at First Symptom.*

If the entire material is grouped according to age (Table 6) at the appearance of the first symptom, it will be seen that on the whole the prognosis is the same in all age groups.

As evident from the tables the prognosis is extremely serious. For purposes of a further elucidation of this aspect Table 7 gives the compensation in per cent. paid by the Directorate of Accident Insurance (1934—42). A comparison with a compensation material of fractures of the carpal scaphoid during the same period reveals that malacia is at least as serious as the former.

Table 7.

108 Cases of Malacia  
(Directorate of Accident Insurance)



Now remains the question of *treatment*:

All definite details as to treatment have been taken from the case records and plotted in Table 8 compared with the functional result. When a case record failed to give definite information about treatment, the case was left out of account.

Among the cases followed up only 3 were treated with plaster bandage for more than 2 months — applied less than 3 weeks after the first symptom.

Thirty-one cases were treated for more than 2 months with immobilization in plaster applied more than 3 weeks after the first symptom.

Fourteen cases were not immobilized in plaster. It will be seen that the functional results are not definitely worse than in the immobilized cases — and the number of cases exhibiting roentgenologic healing is not smaller.

Thirty-nine cases were submitted to operation. Of them one was

Table 8.

*Influence of the Kind of Treatment on the Functional Result.  
(The figures in brackets indicate the healed cases.)*

Plaster bandage more than 2 months	Number	Functional Result		
		Ideal	Good	Poor
Period from 1st symptom to application of bandage				
≤ 3 weeks .....	3	1		2
> 3 weeks .....				
≤ 2 months .....	5 (1)	2 (1)	2	1
> 2 months .....				
≤ 6 months .....	12 (3)	3 (2)	8	1 (1)
> 6 months .....				
≤ 1 year .....	10 (1)	1	6 (1)	3
> 1 year .....	4	1	2	1
Total	34 (5)	8 (3)	18 (1)	8 (1)
Operation .....	39	10	11	18
No immobilization or plaster bandage for less than 2 months .....	14 (3)	2 (2)	8 (1)	4
Treatment unknown .....	5 (1)	1	3	1 (1)
Total	92 (9)	21 (5)	40 (2)	31 (2)

immobilized in plaster from the day after the trauma until operation 9 months later (Case 17).

Let it be mentioned that a definite trauma occurred in 3 of the 4 (3 + Case 17) cases immobilized at once.

Even protracted immobilization in plaster does not — according to the functional result — appear to influence the disease, not either when instituted at an early stage. No doubt, however, the first symptom seldom coincides with the onset of the disease, seeing that the first roentgenogram, as already mentioned, practically always shows changes which must have existed for some length of time. Therefore, it is probably impossible to apply the bandage at the onset of the disease, so that there is actually no way of knowing how an immediate immobilization would work.

It seems fairly certain that even a protracted immobilization instituted when the disease has become advanced is of no demonstrable effect.

Table 9.

Operation	Number	Functional Result		
		Ideal	Good	Poor
<i>Excision of semilunar</i> .....	14	6	6	2
<i>Excision of semilunar leaving a fragment</i> <sup>1</sup> .....	19	3	4	12
<i>Excision of semilunar replaced by fat</i> .....	3	1		2
<i>Excision of semilunar and arthrodesis once</i> .....	1			1 <sup>2</sup>
<i>Excision of semilunar and arthrodesis twice</i> .....	1			1 <sup>3</sup>
<i>Excision of semilunar twice and arthrodesis twice</i> .....	1		1	
Total	39	10	11	18

As regards the *operative treatment* (Table 9) there is a comparatively large number of ideal, but on the other hand also a considerably larger number of poor results than after non-operative treatment. Therefore, this form of therapy cannot be said to improve the functional results. It might though be presumed that operation would as a rule be performed at a late date, when irreparable changes (shrinkage) had occurred in the wrist. Table 10 serves to show that this cannot play an essential rôle, as most of the patients were operated upon before the lapse of the first year from the presumed onset of the disease.

Apart from excision it was in a few cases necessary to perform arthrodesis (Table 9) which, however, does not appear to have improved the condition.

As apparent from Table 11 the procedure of excision may involve the possibility of erroneous removal of other bones — apart from the difficulty in making the excision complete (Table 9). In BÖHLER's opinion these facts reduce the value of this form of treatment to such an extent that he advises against it.

A study of the effect of immobilization on the *radiographic changes* and the relation of the latter to the functional result must be limited to that part of the material which was radiographed at the follow-up (61 cases).

<sup>1</sup> The "remainder" is always demonstrable by roentgen immediately after the excision (in the cases roentgenographed at that time), but the "fragments" are somewhat smaller. Thus, it seems in most cases actually to be a question of small pieces of bone left behind.

<sup>2</sup> Change of occupation. Reduced power.

<sup>3</sup> Change of occupation. Reduced power, swelling.



Table 10.

*39 Cases Submitted to Excision of the Semilunar Bone Set Out According to the Time of the Operation. The Table Also Gives the Functional Result.*

Number of  
Cases of  
Excised  
Semilunar

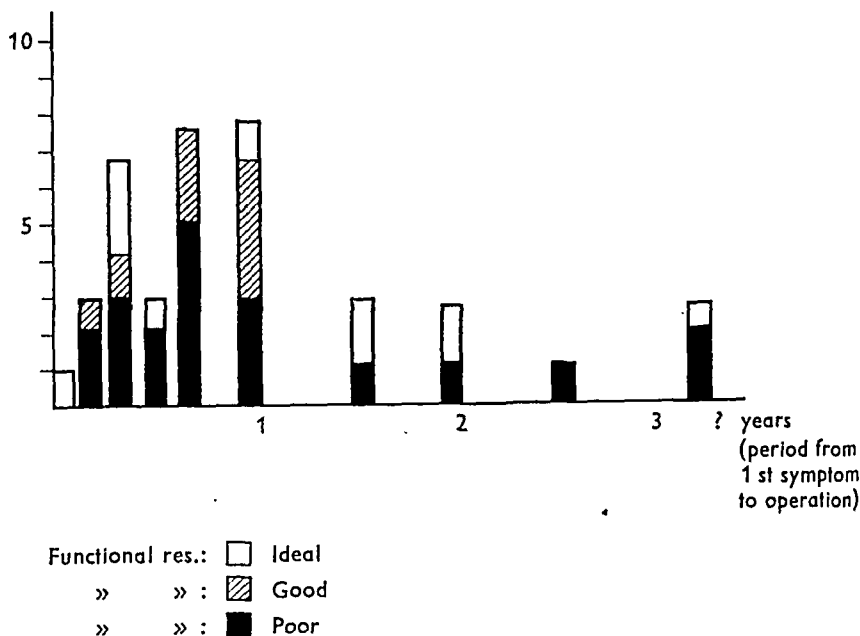


Table 11.

	Number	Functional Result
The excision of the semilunar involved removal of a piece of the os magnum .....	1	Good
Two attempts at removing the semilunar resulted in removal of a piece of the scaphoid .....	1	Poor
Excision of the semilunar involved fracture of the cuneiform .....	1	Ideal
Instead of the semilunar a piece of the os magnum was removed .....	1	Good
Infection and fistula .....	1	Poor

Table 3 sets out the roentgen findings compared with the functional result in the non-operated cases.

Most of the ideal results are to be found among the healed cases, but healing is not tantamount to a guarantee of an ideal functional result. Moreover, there are two cases in which the

Table 12.

*39 Non-operated Cases Followed up by Roentgen Set Out with a View to Influence of Treatment on Healing.*

<i>Plaster bandage for more than 2 months</i>	<i>Number</i>	<i>Healed Cases</i>
<i>Period from 1st symptom to application of bandage</i>		
$\leq 3$ weeks .....	3	6
$> 3$ weeks .....		
$\leq 2$ months .....	4	1
$> 2$ months .....		
$\leq 6$ months .....	10	4
$> 6$ months .....		
$\leq 1$ year .....	7	1
$> 1$ year .....	2	0
<i>No immobilization or plaster bandage for less than 2 months</i> .....	10	2
<i>Treatment unknown</i> .....	3	1
<b>Total</b>	<b>39</b>	<b>9</b>

roentgenologic changes appear to be worse, but still the functional result is ideal.

No distinct difference could be found in the roentgenologic prognosis of the three types of variants.

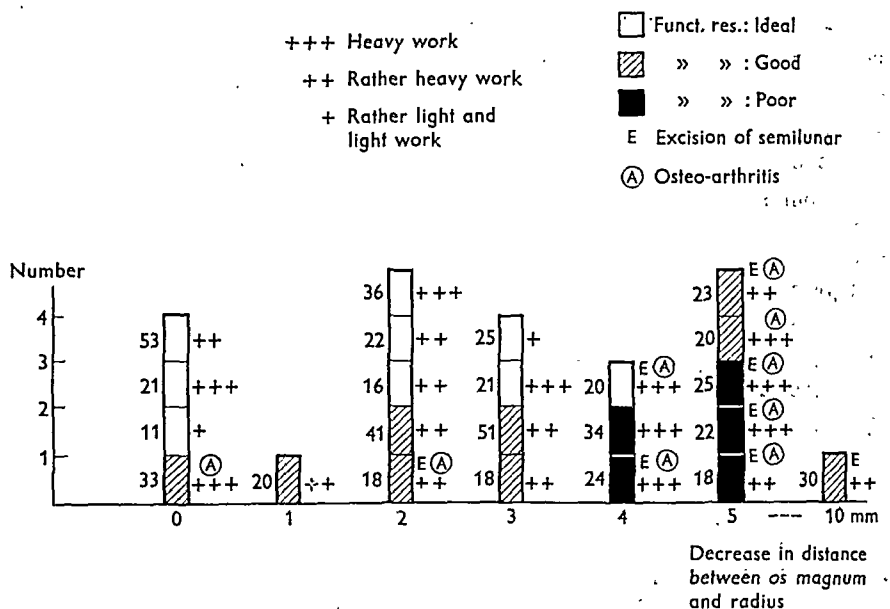
Table 12 gives the influence of treatment on the healing. It will be seen that the number of healed cases does not vary essentially in the various groups.

*The reason of a poor functional result* — even in healed cases could perhaps be sought in *osteo-arthritis*. As mentioned above (see Table 3 and 4) this occurred in 23 of 61 cases. There are, however, only 4 cases of *osteo-arthritis* among the non-operated patients and none among the healed cases. In the cases submitted to excision on the other hand, *osteo-arthritis* was observed in 19 out of 22. A constant connection between *osteo-arthritis* and a poor functional result was not observed — although the former is somewhat more common among the poor than among the “good” and “ideal” results.

A phenomenon which may affect the development of *osteo-arthritis* and which also must be presumed to play an important rôle in the function of the wrist is the more or less marked shortening of the joint attending malacia. STÅHL's investigations strongly suggest that the greater the shortening the poorer is the functional result. In this respect our material is not large as we do not possess roentgenograms of the unaffected side in all

Table 13.

23 Cases in Which a Roentgenogram is Available of the Unaffected Wrist, Showing the Shortening Found at Follow-up.



cases. Still, Table 13 gives the cases in which a roentgenogram is available of the unaffected side for comparison (the shortening is measured as the decrease in mm. of the distance from the proximal part of the joint surface of the os magnum to a point midway between the volar and dorsal edge of the radial joint surface with the hand in the normal-anatomical position).

It is evident that the largest number of poor results are found in the cases of marked shortening, a group which also contains most operated cases — nearly all attended with osteo-arthritis.

When regard is paid to the patients' occupation — also set out in Table 13 — the picture is not essentially altered.

For the purpose of investigating the effect of the patients' occupation on the prognosis in the material as a whole the writers have set out all the cases followed up according to the heaviness of their work (Table 14). As one might have expected a "poor" result is more common among the persons engaged in rather heavy and heavy work, as these subjects predominate among the group who had to change their occupation or change to lighter work within their own occupation. About half these patients had to do so (22 of 55). By way of comparison it must be

Table. 14.

Occupation	Number	Functional Result		
		Ideal	Good	Poor
Heavy work ..... (blacksmith, carpenter, laborer, farmer, joiner etc.)	53	10	21	22
Rather heavy work ..... (brewery worker, factory hand, housemaid, coachman etc.)	23	5	11	7
Rather light work ..... (ticket collector, shop assistant, customs official etc.)	11	3	7	1
Light work ..... (clerk, school boy, slum sister)	3	2	1	
?	2	1	1	
Total	92	21	41	30

mentioned that among 14 patients engaged in rather light or light work, only one has changed his occupation on account of the disease.

It will be seen that malacia is a disease of a most incalculable course which is not definitely amenable to any known method of treatment. Moreover, the functional result of the latter is far from always corresponding to what one might expect according to roentgen findings.

If an opinion on the *treatment* is to be stated nevertheless, it must be to the effect that it can only be considered reasonable to immobilize the wrist in *plaster of Paris* in periods of severe pain and tenderness — *e. g.* following a trauma — not in order to affect the disease itself, but to make the acute state of irritation subside.

A warning must be sounded against excision which, as mentioned above, often seems to make matters worse, because of osteo-arthritis and postural changes in the wrist.

*Arthrodesis* may in a few cases be required because of severe discomfort. Even in cases where this operation is a technical success, it does not infrequently lead to a poor functional result. Therefore the utmost reservation is indicated.

*Shortening of the radius* and lengthening of the ulna do not so seldom entail deformity of the radius and a false joint in the ulna respectively, but otherwise the results appear to be promising.

The writers are unable to suggest any new method of treatment. It should be mentioned here, however, that Sv. KJÆR of the Orthopedic Hospital in Copenhagen has in a few cases of malacia replaced the semilunar bone with a vitallium replica<sup>1</sup> in order to prevent further shortening. The cases have only been followed up for a few months, so that nothing can yet be said about the final result.

### Summary.

After a brief historic review of the pathogenesis, pathology and treatment of lunatomalacia the writers report 109 cases of the condition.

The result of the investigations is as follows:

1) There was a history of a fairly definite trauma in merely 38 per cent. of the cases.

2) The minus variants constitute 42 per cent. of the material, considerably more than usual.

3) The roentgen ray appearance of the *alterations in shape* of the bone varies greatly with the type of variant. The structural changes afford a motley picture. It was impossible to demonstrate a constant initial stage or other typical stages of the course. In 5 cases the radiogram (made from 2 months to 8 years after the 1st symptom) shows changes resembling a compression fracture. In addition all cases show mild changes in the bone. Only in two cases a radiogram was made immediately after a definite trauma — and both exhibit unquestionable changes of long standing.

4) Among 61 cases followed up by roentgen ray (22 of them submitted to excision of the bone) the process is healed in 9. The earliest healing was observed after the lapse of about 2 years. In one case not only the structure, but also the shape has regained its normal appearance.

5) Among *other changes in the wrist*, osteo-arthritis was observed in 23 of 61 cases, 19 occurring among the 22 operated cases. A few instances exhibited a more or less marked subluxation of the carpal scaphoid — and others, with a greatly flattened semilunar

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<sup>1</sup> In 1945 WAUGH & RENLING reported that they had in a few cases of united fracture of the carpal scaphoid replaced the bone with a vitallium replica. No details are as yet available about the end results.

or after its removal, increased density in adjoining bones, esp. the scaphoid. Areas of density in the scaphoid which latter may also be greatly flattened, are particularly marked below the radial joint surface, just as one might expect in view of the altered pressure in the wrist.

In the light of these investigations the writers are of opinion that the interpretation of malacia which ascribes its onset and development mainly to repeated traumas is nearest to the truth.

6) A study of the *prognosis* and *treatment* reveals: 92 of the 109 cases were followed up, 61 of them also with radiograms. Average period of observation 6.6 years.

In a total of 21 cases the result must be described as ideal, 40 as good and 31 as poor (*i. e.* the patient has had to change his occupation or seek lighter work).

Immobilization in plaster of Paris for more than 2 months does not improve the functional result (or the roentgenological) — even in cases where immobilization has been instituted at an early stage.

Excision of the semilunar is the form of treatment which is followed by most poor results.

No constant relation is demonstrable between the roentgen changes in the semilunar bone and the function of the hand, a fact which must be ascribed to osteo-arthritis and an altered posture of the hand. The patient's occupation is of no slight significance to the result as far as working ability is concerned. Although the healed cases are on the whole functionally the best ones, there are also poor results in this group.

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## Multiple Lipoma-Angiolipomas.

By

KRISTIAN KROHN KLEM.

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This article is a discussion of a disease which is seldom seen in its multiple form, though it can hardly be called a rarity. Three patients are reviewed. The first had consulted several doctors without receiving help. The other two were brother and sister whose deceased father was said to have had the same disease.

The first patient was a 19-year-old farm hand. Several years previously he had noticed a lump on the back of the right hand. Over a period of a few years he developed lumps here and there on his body. Many of them had become tender, and there were times when he had severe back pain which he thought had some connection with his tumors. He complained of marked sweating from the back during the last few months. 39 visible or palpable tumors were found on the abdomen, back and extremities at physical examination. (Fig. 1—4.) It was noted that there were no tumors on fingers, toes or around the nails (as found in glomus tumors). The tumors varied in size from that of tiny peas to walnut size. Most of them were soft and elastic, some more firm than others. Some of the larger tumors were tender upon pressure. The large tumors in the lumbar region were visible through the skin because of their bluish color. A biopsy was taken from the volar surface of the right forearm on Dec. 19, 1946. The report from the pathologist, Dr. R. EKER, was as follows (Fig. 5—6): "Tissue the size of a coffee bean received. Microscopy reveals a lobulated tumor partly encapsulated but only partly circumscribed. It is highly cellular dominated by a wealth of capillaries. These are covered by blood vessel epithelium and with large spindle shaped or polygonal cells which lie close together and have marked borders composed of cytoplasm. These cells may be changed muscle cells or in part blood vessel epithelium. The nuclei are oval and of varying size and chromatin content. They are not grossly atypical nor are there many mitoses. There are a number



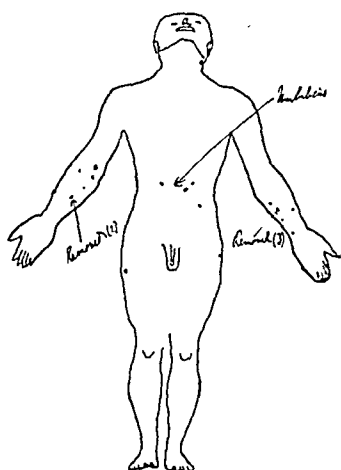


Fig. 1. The scar remaining after the biopsy from the right forearm and 4 tumors are seen.

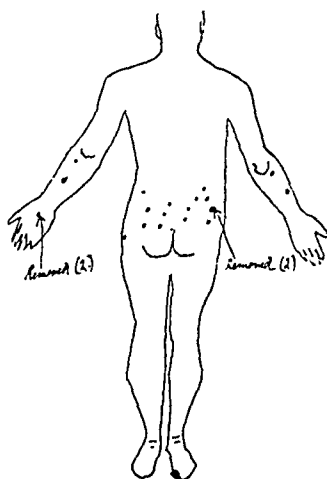


Fig. 2. Tumor from the right hand back.

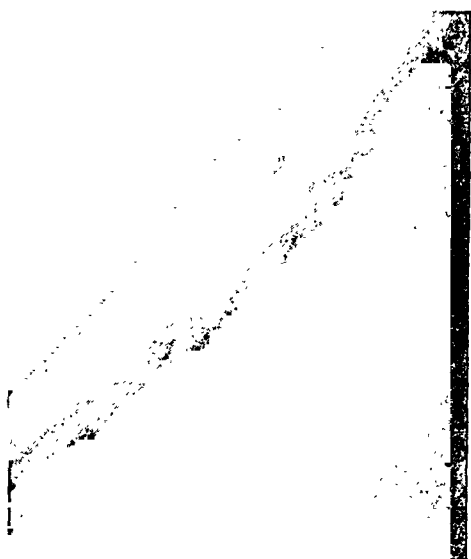


Fig. 3.



Fig. 4.

of thick-walled blood vessels around the borders of the tumor. No nerve tissue was found. The specimen is an angioma, and, although it is not typical, it appears most likely that it is a *glomus tumor*." (Fig. 7, 8.)

The clinical picture coincides also in part with this diagnosis.

Another biopsy from the right lumbar region was performed later after the patient had consulted an internist who interpreted the disease

as Recklinghausen's disease. The biopsy report from the same pathologist, Mar. 14, 1947, was as follows (see second photomicrograph): "An encapsulated piece of tissue the size of a plum was received. Microscopic diagnosis: *Lipoma*. P. S. The tumor received previously was reexamined. The reader is referred to the description given before with the addition that the tumor contained a small amount of fatty tissue. In connection with the fact that the patient has multiple tumors, the picture in this tumor indicates that it is an angioliipoma completely dominated by the proliferation of blood vessels. I have seen a slight tendency to the same type of blood vessel proliferation in the usual lipoma upon occasion, though not a similar picture, and I believe that this case may be of especial interest. If possible it would be interesting to examine more of the tumors. Do they show different consistence and color?"

The third biopsy was taken from the anterior surface of the left arm. The biopsy report, March 25, 1947, from D. R. EKER was as follows (see the third photomicrograph): "Encapsulated tissues, one the size of a pinhead and one the size of a bean were received. Microscopic examination showed a rather well circumscribed tumor composed mostly of fatty tissue. There are no markedly atypical nuclei. In several places, particularly in the periphery, there are large numbers of capillaries. They are covered with the usual blood vessel epithelium, and between them there are spindle shaped or polygonal cells which seem to be partly proliferating epithelium and partly fibroblasts. These forms are not notably atypical. The increased number of blood vessels is so marked that it seems probable that this also has played a part in the development of the tumor. Diagnosis: *Angioliipoma* (lipoma teleangiectaticum). (Fig. 9, 10.)

I have not previously seen so varied a picture of angiomas, lipomas and combined forms of both. This condition is doubtless a *variation of multiple lipoma*."

Two similar cases, interesting because there appears to be a familial tendency, are reviewed below. The histologic diagnosis in these cases was clear from the beginning. The patients were siblings, brother and sister, 48 (Fig. 11, 12) and 46 years (Fig. 13, 14) of age. Their father, who died at the age of 82 had also had "lumps" on his body and extremities. There were no other known cases of the disease in the family. The clinical and histologic pictures were similar in the brother and sister. There was also remarkable likeness in the number, localization, consistence and size of the tumors. Some of the "lumps" were occasionally quite tender, but neither of the patients had suffered pain which could be laid to the disease. The first tumors had appeared many years ago, and new tumors had developed at intervals up to the present. They approximated lipomas in consistence, some softer and some harder. They varied in size from the size of a pea to a plum. The localizations are shown in the accompanying drawings.

A tumor was removed from the left thigh and the left wrist of the man. The biopsy report was as follows: May 5, 1947, by Dr. med. R. EKER. "Diagnosis: *Lipoma*." The author notes the following in the

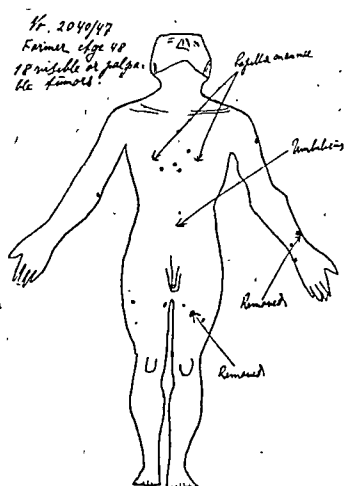


Fig. 11.

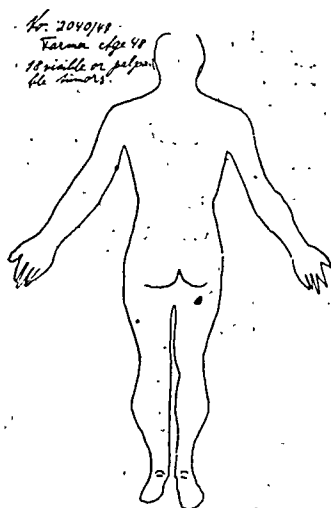


Fig. 12.

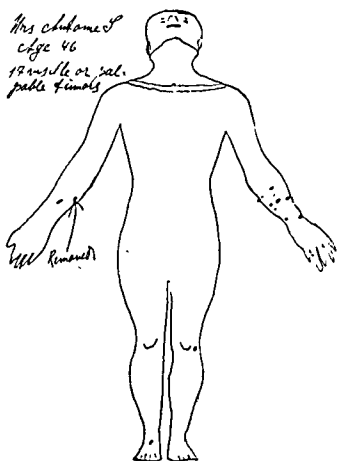


Fig. 13.

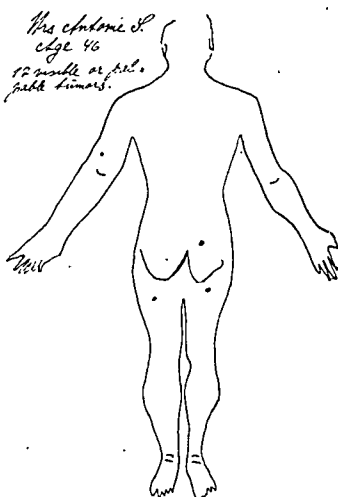


Fig. 14.

description: "Small fatty cysts surrounded by lipid macrophages and giant cells of a type associated with foreign bodies are also seen."

A tumor was removed from the volar surface of the right forearm of the sister. Biopsy report June 21, 1947, by Dr. med R. EKER was: "*Lipoma.*" The description included the following: "The biopsy tissue contains narrow traces of connective tissue. These in turn contain many capillaries and some proliferation of blood vessel epithelium. However, the vessels do not dominate the picture."

A complete discussion of this disease is to be found in EWING'S "Neoplastic Diseases".

Certain facts concerning multiple lipomas have bearing upon the cases reviewed here. Many factors appear to figure in the etiology. MURCHISON discusses a family in which the father and

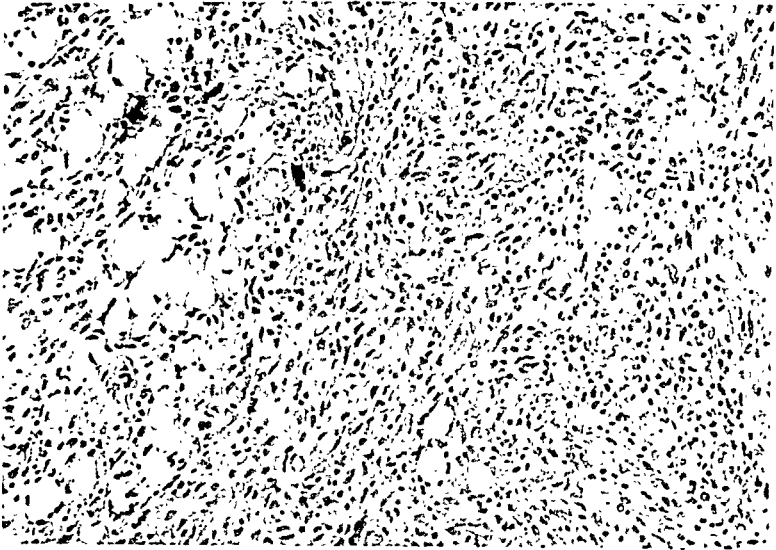


Fig. 5.

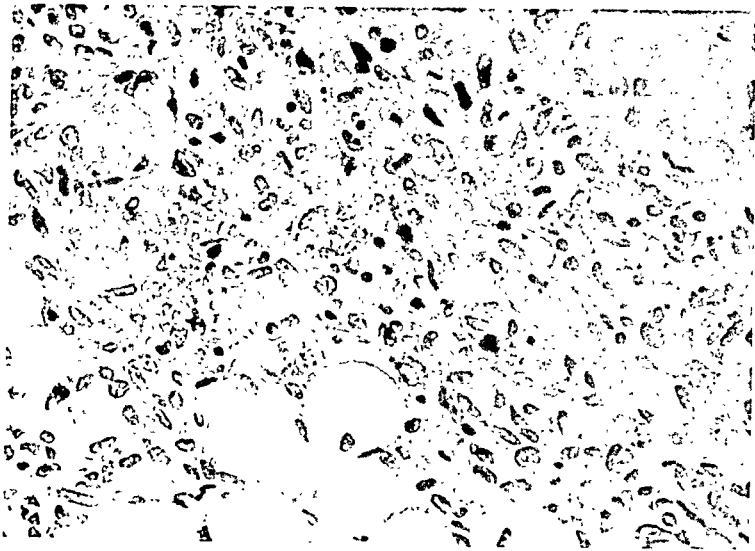


Fig. 6.

Tumor from the volar surface of the right forearm. Full description is found in the text. Note the dominating proliferation of blood vessels and the large numbers of spindle shaped or polygonal cells which led the histologist to make the diagnosis of glomus tumor. A small amount of fatty tissue, overlooked at the first examination, is also seen.

Diagnosis: (Glomus tumor) Angiolipoma.

KLEM: Multiple Lipoma-Angiolipomas.

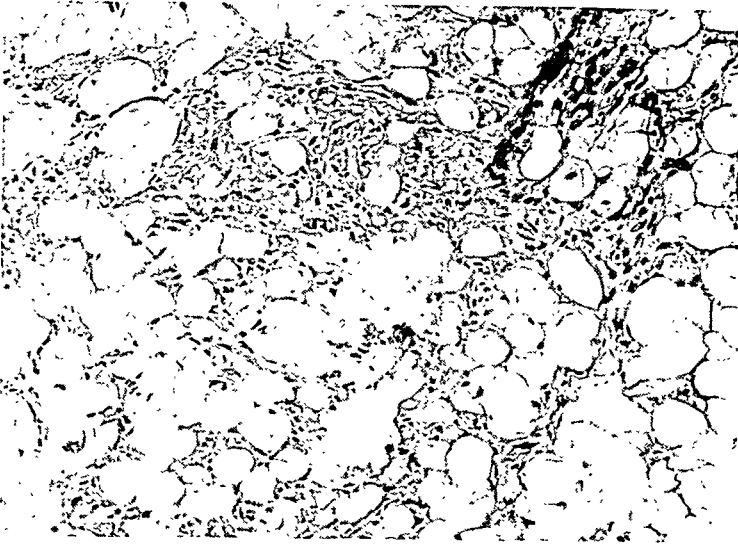


Fig. 7.

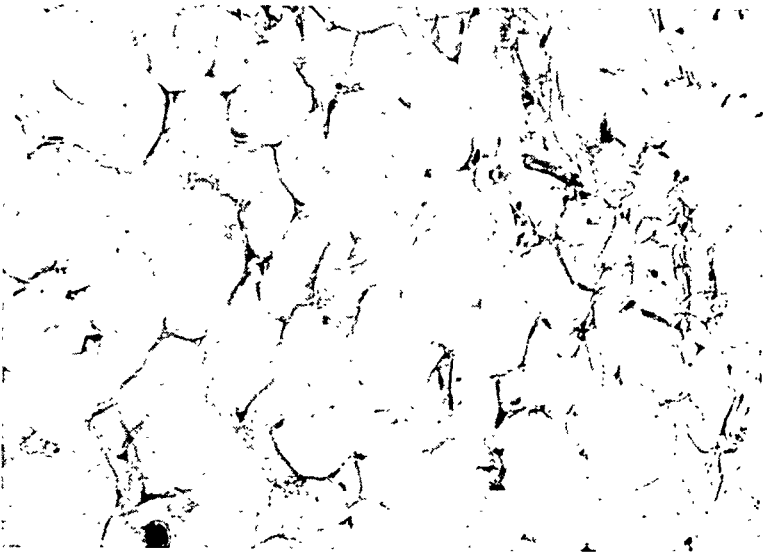


Fig. 8.

*Second photomicrograph* (high and low power). Tumor from the back. See the description by Dr. med. R. EKER in the text.  
Diagnosis: Lipoma.

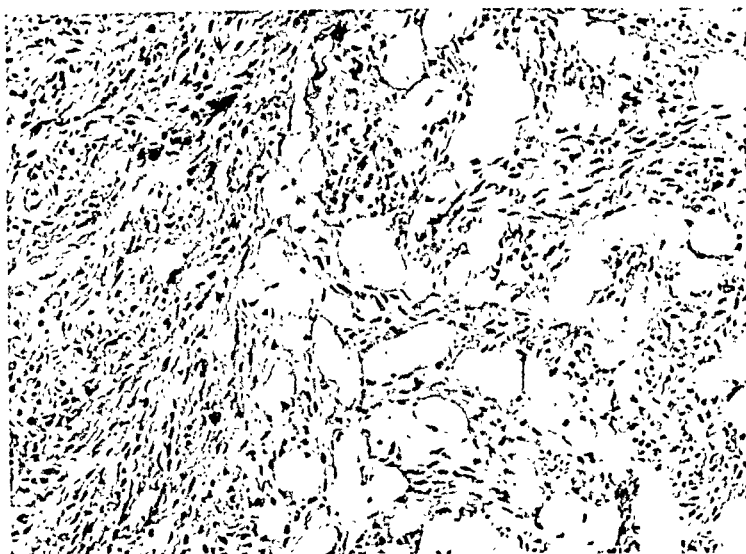


Fig. 9.

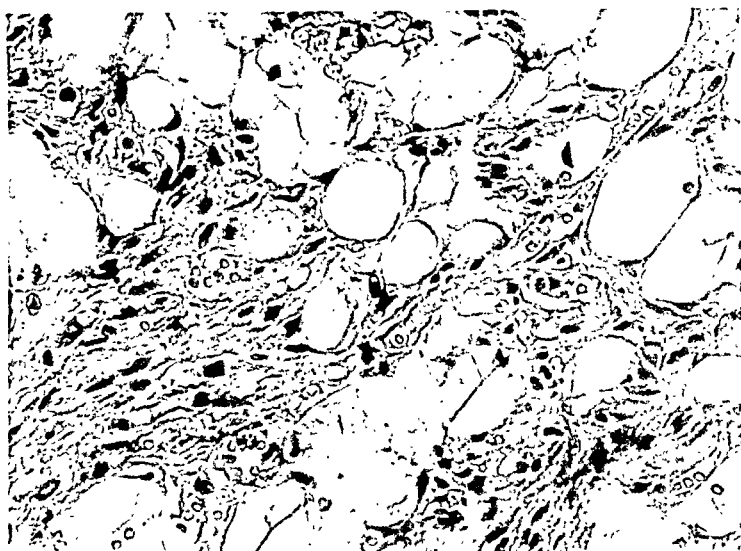


Fig. 10.

Tumor from the volar surface of the left forearm. See the description by Dr. med. R. EKER in the text.

Diagnosis: Angiolipoma (lipoma teleangiectaticum).

KLEM: Multiple Lipoma-Angiolipomas.



three daughters had multiple symmetric lipomas while nine sons had none. BLOSCHKAS reports a family in which only the men were affected, and the first symptoms appeared at puberty. MEERBECH and PETRÉN also discuss cases in which heredity was a factor. PAYR and KOETTNITZ, among many other authors suggest that the occurrence of multiple symmetric lipomas is connected with the peripheral nerves. In a number of cases the tumors are painful and accompanied by other nervous system phenomena. ALSBERG found numerous neurofibromas together with many lipomas in the same patient, and he followed the nerve fibers into some of the lipomas. However, the occurrence of lipomas together with neurofibromas is extremely rare, and it has not been possible to prove a relationship between the lipomas and the peripheral nerves, as is found in fibromas. True lipomas are most probably connected with diffuse or local fatty tissue proliferation which has the same relation to the lipoma as diffuse fibromatosis has to the fibroma. In individuals who may be supposed to have a local or general predisposition, trauma may cause solitary, superficial lipomas. A congenital predisposition of the tissue is accepted as an essential factor in the cause of lipomas.

VIRCHOW claims that the occurrence of multiple lipomas, even by the hundred, is an expression of a peculiar pathologic predisposition of the fatty tissue in the persons affected, in whom the tumors may appear in the lungs and liver where fat is not normally found.

Continued recurrence of lipomas is rare and usually associated with cell, blood vessel or sarcomatous structure.

The microscopic picture is often marked by fields of polygonal cells containing incomplete fatty depots. Growth of the lipomas most often occurs from such cells, which lie in isolated fields or along the blood vessels. In some of these places the polygonal cells form an alveolar structure. Blood vessels are usually found in large numbers, and many arterioles in the stroma may be seen to enter the lobes and divide into capillaries. If there are more than the usual numbers of blood vessels, they may cause the formation of vascular fatty tumors, lipoma teleangiectaticum or cavernosum. It is difficult to differentiate between vascular lipoma and angioma. The lymphatic vessels may also be overdeveloped. BORST observed the transformation of a lipoma to a fibrous lymphangioma. Fatty cysts containing fluid fat may also be found in lipomas. These are thought to be caused by trauma.



### Summary.

The first case discussed is an example of the difficulty of diagnosis, both clinical and histologic in a benign tumor disease. The problem of differential diagnosis versus the interesting so-called glomus tumors is noted. After the probable diagnosis glomus tumor was made on an histologic basis, there was a temptation to associate the patient's pain and sweating with the tumors. Further examinations show a varying histologic picture of several tumors from the same patient. The other two cases discussed appear to have a familial predisposition to the disease. Certain general remarks concerning multiple lipomas are included.

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EWING, JAMES: Neoplastic Diseases, p. 191.

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## **Does Any Genetic Connection Exist between Pyloric Hypertrophy in Infants and in Adults?**

By

LENNART ZETTERGREN.

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Apart from the infantile pyloric hypertrophy, which constitutes the patho-anatomical basis of the more generally known term of pylorospasm, a pyloric hypertrophy of an "essential" nature occurs in adults. From having been practically ignored in Scandinavian literature, the pyloric hypertrophy in adults has, in recent years, attracted more and more attention. Thus, in 1946 this disease was made the subject of discussions both in Danish and Swedish quarters (ANDERSEN, GAMMELGAARD & DE FINE LICHT; ZETTERGREN). Even though better known at the present time than formerly, a brief account of the symptomatology and pathological anatomy of the disease may be justified.

Pyloric hypertrophy in adults is by no means rare, at any rate from the point of view of the pathologist. Mild forms of hypertrophy are not seldom observable as by-findings at post-mortems. To the roentgenologist, who most often discovers the disease only at its full development, the frequency appears considerably lower. The disease occurs most often in elderly people. Thus, the mean age of the 22 cases observed by the present writer is about 60 years, a figure well conforming to that of ANDERSEN and co-workers (8 cases). The disease seems to be more frequent in men than in women. Approximately 70 per cent of the cases recorded in the literature apply to men. The disease histories often report stomach troubles, in the form of pains and a feeling of soreness in the pit of the stomach, eructation and vomiting, and, further, lack of appetite and loss of weight. In the majority

of cases, examinations of the gastric juice disclose low values of acidity and, not rarely, achylia. The roentgenological picture varies rather, and it is not always easy to interpret it. *In most instances, the patient is subjected to operation on a suspicion of cancer or peptic ulcer.* Occasionally, however, the roentgen picture suggests that of infantile pyloric stenosis. ANDERSEN and co-workers stress the following characteristic findings:

1. Variations in the width of the constricted part.
2. The absence of irregular arrosions.
3. A contrast-filled cleft between the pyloric sphincter and the rest of the hypertrophied area.
4. The presence of the mucosal folds.
5. A small, palpable, mobile tumour.
6. A rounded, mushroom-like defect in the base of the bulbus.

Patho-anatomically the disease manifests itself in a more or less pronounced thickening of the wall in the antral part of the stomach ("canalis egestorius"). As in infants, the hypertrophy chiefly affects the inner circular layer, which sometimes will measure up to 10 or 12 mm in a transverse section. Typical features of the hypertrophy is an extremely sharp delimitation towards the duodenum where it suddenly terminates, while, in the ventricular direction, it gradually fades out up towards the oral part of the pyloric canal. The sphincter itself does not, as a rule, form the seat of any particularly conspicuous hypertrophy (ANDERSEN and co-workers). On the other hand, contrary to the infantile form, the pyloric sphincter itself is but rarely found to be distinctly severed from the hypertrophic musculature of the pyloric canal. In a majority of cases, signs of chronic gastritis, with a distinct fibrosis of the submucosa and the muscularis, is noticeable, both macro- and microscopically. From the above description of the patho-anatomical picture of pyloric hypertrophy it is evident that the term pyloric hypertrophy is in no way adequate, seeing that such a term should, properly, apply to an isolated hypertrophic development of the sphincter pylori itself. Consequently, the disease should be called muscular hypertrophy of the pyloric canal. The affection has, however, long been termed pyloric hypertrophy and, for that reason, the term may be retained.

Before entering on a discussion of the various opinions regarding the nature of pyloric hypertrophy, it seems appropriate to submit some brief remarks also concerning the symptomatology and patho-

anatomy of the infantile form of the disease. Mostly, it occurs in the 3rd or 4th week of life in healthy and strong breast-fed children, being decidedly more common in boys than in girls. The most striking symptom is intense, explosive vomiting fits. Often, the amount of vomited matter exceeds that of the last meal. Thus, a retention occurs, a fact verified by roentgenological examinations. For the rest, the clinical picture is characterized by pseudo-obstipation, oliguria and pronounced loss of weight. Often, a distinct ventricular peristalsis is seen through the abdominal wall and the thickening of the pyloric region can, not seldom, be palpated as a torus, the size of a fingertip. Roentgenologically, the disease displays a typical picture. According to RUNSTRÖM, the lumen of the pyloric canal has, at its manifest stage (stage I), the shape of an exceedingly narrow canal of a length of approximately 2—3 cm. The stomach discloses a stenosal peristalsis which does not pass through the contracted area. The opening time is prolonged. At the non-manifest stage (stage II), which may last for 4 years or more, the lumen of the pyloric canal widens and remains open for a normal length of time, though the peristalsis stops at the hypertrophic part. At the last stage (stage III), which may continue up to an age of 13 years, light peristaltic waves become visible in the canal. RUNSTRÖM has ascertained the interesting fact that a patient may roentgenologically disclose changes, corresponding to those of stage II, without revealing any clinical symptoms. — Patho-anatomically, the disease manifests itself as a concentric, firm thickening of the wall of the canalis egestorius. The lumen of the pyloric canal can have the fineness of a probe. Histologically, the thickening is found to be contingent to a hypertrophy of the muscularis propria, particularly of its inner circular layer. In the muscularis no infiltration of round cells of cicatricial tissue is to be noticed (MONRAD). On the other hand, the mucosa and submucosa are, as a rule, somewhat thickened.

The etiology and pathogenesis of pyloric hypertrophies are still obscure. Even in modern text-books, the *infantile form* is often designated as *congenital* pyloric stenosis. However, as demonstrated by RUNSTRÖM, this idea of the supposed congenital nature of the disease, is probably mistaken. With a view to ascertaining the existence of any anatomico-roentgenological pre-stages in the disease, in children who at a later time became affected, RUNSTRÖM examined 1,000 infants 3—6 days after

birth. Since the disease, as previously mentioned, is considerably more frequent among boys than among girls, boys were, in the first place, subjected to examination. Girls were examined only when older children of the same family had been attacked by the disease, considering that it is pronouncedly familial. However, on the occasion of this investigation, no definite pathological changes could be detected in the examined children. None the less, 5 children returned with clinically typical symptoms, all of them having, as stated, at the first examination disclosed entirely normal roentgenological pictures. According to RUNSTRÖM, the result of his investigation warrants the conclusion that "children who are afterwards affected by the disease do not show any roentgenological changes, when examined 3—6 days after birth, and that for this reason, *the disease is not congenital*". These observations of RUNSTRÖM's are, no doubt, of great value, principally because they offer a useful basis for future research but, unfortunately, they do not provide any answer to the question of the origin of this peculiar disease.

With regard to the pathogenesis of *pyloric hypertrophy in adults* two opposite views have been urged. On the one hand, the hypertrophy in adults is placed in relation to that of infants, being interpreted as a persistent infantile form (CRYMBLE & WALMSLAY), while, on the other hand, it is supposed to be an entirely independent morbid condition, acquired during the later part of the life of the individual (RUNSTRÖM, ZETTERGREN). The fact that pyloric hypertrophy in adults chiefly occurs in males undeniably speaks in favour of the first contention. This conformity between the two diseases seems, however, to be the only one. The lingering, often "lifelong", gastric troubles cannot be quoted as evidence of any connection with the infantile hypertrophy, seeing that chronic dyspeptic complaints frequently appear at a very early age. Also, the clinical pictures are essentially different. While the symptoms, in the case of pylorospasm, are acute, extremely typical and gradually disappearing, they are, in so far as hypertrophy in adults is concerned, surreptitious, diffuse and, as in the instance of dyspeptic complaints, not seldom disclosing seasonal variations. Further, it would seem rather strange, should a disease acquired at the earliest infancy proceed without any symptoms whatever up to, mostly, an age of 50—60 years, only then to reveal any sign of its presence. While the roentgen picture is strikingly typical in the infantile form of the disease, it is, in the case of

a hypertrophy in an adult, exceedingly variable and often difficult to interpret. Occasionally it conforms to that of infantile hypertrophy, though this happens only exceptionally. However, the most substantial reason against a supposed connection in the development of these two diseases is provided by MONRAD, through his observations at post-mortems of such children as have been treated for a typical pylorospasm, for varying periods of time before the autopsies. MONRAD was in a position to dissect five cases of children who had been under his personal treatment for this disease and recovered, and who afterwards died in other illnesses. At their second admission to the hospital, roentgenograms of these five children disclosed no signs whatever of morbid changes in the stomach. The autopsies resulted in the following observations: In a child that died one month after having been cured from its pylorospasm the conditions of the pyloric canal were exactly the same as those of a child that dies during the florid stage of the disease. In two children who died two months after the termination of the clinical symptoms a still typical transformation was discovered in the pyloric canal, though with a considerably reduced thickening of the muscularis. In another child, deceased 6 months after recovery from a severe pylorospasm, no typical deformity was observed in the pyloric canal, but the musculature still had a cartilaginous hardness and was somewhat thickened (3 mm). And, finally, both the sphincter and the pyloric canal were found to be completely normal in a child that died in miliary tuberculosis a year and a half after the clinical recovery from a particularly severe pyloric stenosis. These observations of MONRAD's have been confirmed in other quarters. They conform well with the results of RUNSTRÖM's roentgenological investigations. It is, thus, evident that *an infantile hypertrophy will disappear with advancing age.*

Consequently, there is much that speaks in favour of a contention that a *pyloric hypertrophy in an adult has no genetic connection with the infantile form.* The present writer has, on earlier occasions, expressed that opinion, while emphasizing that a chronic gastritis may, very conceivably, be of some significance with regard to the origination of the disease. In support of this hypothesis may be quoted the fact that a majority of cases of pyloric hypertrophy in adults disclose more or less pronounced signs of chronic gastritis, clinically as well as patho-anatomically. It should, however, be kept in mind that, in some instances, such

a gastritis may, possibly, have originated in a retention arising from a pyloric stenosis and, accordingly, be secondary to the hypertrophy (a so-called retention gastritis). Also, in judging the part played by a gastritis in the initiation of a disease, regard has to be paid to the fact that, in patho-anatomically mild forms, this morbid condition is extremely common in this particular region of the stomach (antral gastritis). However, far from all pyloric hypertrophies reveal any stenosis and, this notwithstanding, gastritis symptoms will in such cases be found clinically and histologically grave enough to make it difficult to eliminate the supposition that, in some way or other, the chronic gastritis possesses a significance with regard to the pathogenesis of the disease. The question then arises of such possibilities as may offer themselves for investigating more closely the part of the primary gastritis in the origination of a pyloric hypertrophy. This would appear to be feasible in the case of such patients as have fallen prey to a severe gastritis by swallowing some acid or lye. The fact that such an occurrence will actually produce gastritis of a pronounced type seems to be established by histological examinations of the stomach of patients who have died after having swallowed acid or lye (FRANZAS and others). Within the stomach, injuries particularly from acids are known to be located, preferably, to the pars descendens and pars pylorica (ORATOR, BIERING). Provided that the hypothesis propounded by the present author be correct, a pyloric hypertrophy, of the same appearance as that of the "essential" ones, should prove ascertainable, roentgenologically as well as at autopsy, within a certain limit of time from the occurrence of the injury. The present author has been able closely to study two cases in which acids had been swallowed, both, it will appear, being of interest from the point of view of the significance of a gastritis with regard to the origination of a pyloric hypertrophy.

*Case 1.* Hulda S. 46 years of age. *Clinical diagnosis:* *stenosis cardiae* (caustic damage); *psychosis mano-depressiva*. Previously on the whole healthy. On March 9th 1946 the patient, with a view to committing suicide, swallowed four table-spoonfuls of hydrochloric acid. Vomited at once. Afterwards drank a lot of milk. The patient became deeply depressed, refusing to eat. On March 29th the esophagus was roentgenographed. The passage was without remark. On April 12th 1946 the patient was admitted to Ulleråker's Hospital under a diagnosis of manic-depressive psychosis. Refused to take other than liquid food. A drop enema containing glucose was administered. The patient



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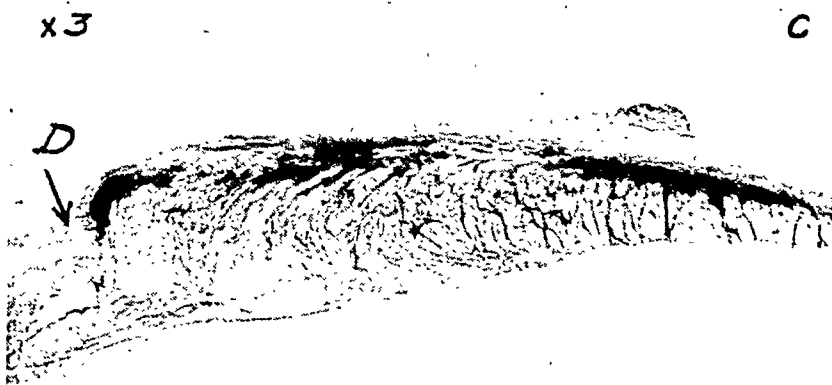


Fig. 1. c) Pronounced pyloric hypertrophy of the same type as the previous case. Marked fibrosis in the submucosa and the muscularis (Case 1).

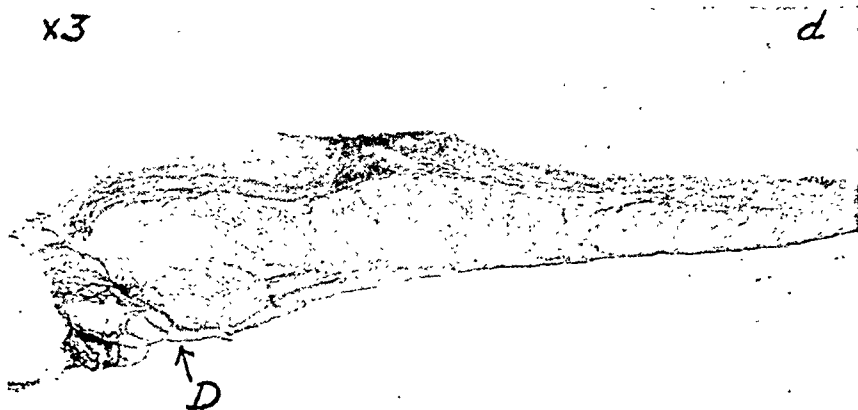


Fig. 1. d) Typical pyloric hypertrophy with conspicuous fibrosis in the submucosa (Case 2).

D = the beginning of the duodenum. In all instances magnification of about 3 times. v. Gieson.

steadily lost weight. Quantity of urine secreted in 24 hours amounted to 300—700 cc. On May 13th 1946 transferred to the Medical Clinic of the Academic Hospital at Uppsala. Then complained of stomach ache. Could take only liquid food, injected per rectum. Ventricle roentgenographed on April 30th 1946: Stomach small, markedly deformed. The contrast medium passes the cardia with little difficulty. The deformity manifests itself in a pronounced shrivelling, on the side of the *curvatura minor*, and a *peculiar contraction of the pyloric canal*. Esophagoscopy on May 24th. Mucous membrane of ordinary paleness. The probes pass without any difficulty through the cardia. After her discharge from the Medical Clinic the patient was readmitted to Ulleråker's Hospital where, on August 20th 1946, she suddenly died. Autopsy disclosed an abscess, the size of a hen's egg, in the right lung, as well as an intense purulent bronchitis. In its lower part the esophagus displayed a pronounced thickening of the wall. The mucous membrane was pale, the surface here and there slightly granulated. The cardia was constricted, the diameter of the lumen being 3 mm. The stomach was reduced, with a moderate thickening of the wall, especially on the side of the *curvatura minor*. The mucous membrane everywhere pale, and, particularly in the thickened area, thin and atrophic and firmly fixed to the underlying stratum. The pylorus was constricted, with a lumen of approximately 5 mm. The musculature in the pyloric canal pronouncedly thickened, measuring about 7 mm, of a fibrotic appearance. The duodenum without remark. The peritoneum everywhere smooth and shiny.

*Microscopic examination* (the pyloric canal): The mucous membrane in the pyloric canal is found to be conspicuously thin and atrophic and, here and there, fibroid with a sparse infiltration of round cells. The submucosa markedly sclerosed, but only to a slight degree affected by any inflammatory cellular infiltration. In its juxtapyloric part it seems somewhat thickened. Among the findings a pronounced hypertrophy, in the inner circular muscular layer in the distal part of the pyloric canal, altogether predominates. This hypertrophy reaches its maximum on a level with the pylorus, terminates, with a sharp delimitation where the duodenum begins, while gradually fading away towards the proximal part of the pyloric canal. In its thickest portion the musculature is 6.5 mm in a transverse section. It forms the seat of a pronounced fibrosis. The streaks of connective tissue proceed from the submucosa, continuing in thick or fine lines, with infiltrations of round cells, between the muscular bundles of the propria. The pyloric sphincter without remark. No signs of peptic ulcer or ulcer scars in any of the sections.

*Case 2.* Gunnar E. 27 years of age. *Clinical diagnosis:* *Tbc. pulm. amb. c. pnthx. art. dx. + Tbc. intestin. + Amyloidosis + Polyarthritis chron.* Arthritis troubles since his eleventh year of age. The tuberculosis detected in 1944. He was then admitted to the Central Sanatorium at Uppsala. In the hospital records, he is stated to have been operated upon in the stomach after, at the age of two years, having swallowed some hydrochloric acid. Unfortunately, a more precise specification

of time has proved unavailable. On the 16th of August 1946 the patient died in his lung tuberculosis. *Autopsy*: the esophagus without remark. The stomach of ordinary size and form. A gastro-enterostomy with an opening with a diameter of four fingerbreadths. The mucous membrane of the stomach is, here and there, somewhat red-stained, but everywhere thin, and can be lifted in folds. In the distal part of the pyloric canal the musculature is markedly hypertrophic. In the section it has the usual appearance and does not seem fibrotic. The lumen of the pylorus has the breadth of a pencil. The musculature of the pyloric sphincter without remark. In the first part of the duodenum plenty of digested food. No peptic ulcers or cicatrices observable. *Microscopic examination* (the pyloric canal): The mucous membrane somewhat atrophic but disclosing no signs of the presence of inflammation. The submucosa displays a pronounced fibrosis and a slight infiltration of round cells but is otherwise without remark. The muscularis is distinctly thickened, in its thickest place measuring 7 mm in a transverse section. The hypertrophy reaches its maximum close to the pylorus, gradually fading out towards the oral part of the pyloric canal. The musculature forms the seat of a moderate fibrosis. No ulcers or delimited cicatrices discoverable in a number of sections from different parts of the pyloric canal.

Without doubt, the forementioned cases of pyloric hypertrophy have occurred as a result of the action of the acid on the ventricular wall, *i. e.* consequent on a diffuse, cicatricial gastritis of the pyloric canal. The striking similarities with regard to the patho-anatomical changes between the hypertrophies originating from "the acid-gastritis" and the more essential ones speak in favour of a pathogenesis common to both. For this and other reasons it seems likely that a *chronic gastritis constitutes the source from which a pyloric hypertrophy in an adult originates*. To this contention the objection may, perhaps, be raised that, considering the exceedingly high frequency of chronic gastritis, the pyloric hypertrophies should, under the forementioned supposition, be far more common than they are. However, as previously stated, mild forms of hypertrophy are by no means rare. As pointed out by NICOLAYSEN, a certain degree of thickening of the ventricular wall of the antrum will extremely often be noticed in cases of chronic gastritis with ulcer symptoms.

However, even though a chronic gastritis may, with a considerable degree of probability, be supposed to form the cause from which a pyloric hypertrophy arises, it seems fairly difficult to explain the precise mechanism of the pathogenetic connection. From a purely theoretical standpoint, a hypertrophy of the type

discussed here should originate either 1) in order to compensate for an organic or functional stricture in the pyloric sphincter itself or 2) as a result of a protracted or iterative spastic contraction in the musculature of the pyloric canal.

As far as the first alternative is concerned, there is nothing to say in favour of it. The histological findings contradict a supposition of an organic stricture in the sphincter. They show that, contrary to the musculature of the pyloric canal, that of the pyloric sphincter is always exempt from any fibrosis. On the other hand, the fact, observed also by ANDERSEN and co-workers, that the pyloric sphincter does not display any signs of hypertrophy, speaks against any assumption of a functional sphincteral stricture, *i. e.* a spasm.

As regards the hypothesis that a chronic spasm in the musculature of the canal may cause the hypertrophy, it has been ascertained that such a spasm does not seldom occur. For instance, in a case of relative pyloric stenosis, published by PRINZ, the antral part of the stomach was, at operation, found to have a reddish appearance. At a slight touch the musculature reacted with a local, extremely marked contraction. The present writer has previously reported a case of pyloric hypertrophy in a man of 64 years of age with a disease history of 6 months. At the operation the distal part of the pyloric canal was seen to merge in a greyish-white, firm tumour, the size of a walnut, which, under the disengagement of the duodenum, considerably diminished. Accordingly, the not infrequent occurrence of a spasm in a thickening of the musculature in the pyloric canal can hardly be denied, but whether it be primary or secondary to the hypertrophy cannot be definitely decided. However, certain observations suggest that it is primary. A case of bronchial asthma and pyloric hypertrophy in a woman, 36 years of age, published by SANDELIN sheds an interesting light on this problem. Simultaneously with asthmatic attacks, the patient often felt abdominal pains and, because of the latter symptoms, she was admitted to a hospital. At the subsequent examination a tumor, the size of a plum, which at the operation was seen to consist of a thickening of the pyloric region, was palpable to the right of the epigastrium. The pyloric canal was extremely narrow but the mucous membrane seemed normal and was mobile against the underlying musculature, which was strongly thickened, measuring 16 mm transversely. The histological examination disclosed an infil-

tration of, chiefly, eosinophilic leukocytes, sparse in the submucosa but exceedingly marked in the musculature. The musculature displayed "degenerative processes". In this instance there is no reason to doubt that the spasm is primary to the hypertrophy. In all likelihood, the same applies to other cases. In his discussion of the nature of the hypertrophy SANDELIN also stresses the possibility that the pyloric stenosis in the forementioned case "is of the same nature as the stenoses in the bronchi in asthma".

Now, the question of *the causes* of this spasm presents itself, for very likely, there is more than one cause to be looked for. Unfortunately, the histological examination offers no more of an answer in this instance than in the case of most visceral dyskinesias. One theoretically feasible possibility, with regard to the origination of a spastic state of contraction in the musculature of the pyloric canal, is that the inflammatory products arising from the chronic gastritis play the part of allergens causative of spasms in a pathergic. Thus, the hypertrophy should originate in a way similar to that of bronchial muscular hypertrophy in bronchial asthma. — Also another possibility offers itself, viz., that the fibrosis has changed the normal conditions of motility of the stomach, and more especially of the pyloric canal. This is due, partly, to the fact that the mucous membrane cannot function to the same extent as normally, irrespective of the muscularis, since it has become more fixed to the submucosa and, thereby, to the muscular wall, because of the abnormal mutual fixation of the muscular bundles, and, partly, from unavoidable defects owing to contractions of the musculature. Such changed and abnormal conditions of motility in one of the most important parts of the stomach, *i. e.* "canalis egestorius", may very conceivably cause a muscular hypertrophy of a compensative nature.

Finally, to return to the question expressed in the headline of this paper, viz.: "Does any genetic connection exist between pyloric hypertrophy in infants and in adults?", it should be evident, from the arguments set forth above, that in the opinion of the present author, no such connection exists between these two diseases. This implies no denial of the fact that similar or identical etiological factors may be significant with regard to the origination of both these diseases (*cp.* the allergic theory of the present author). Only careful follow-up examinations of a com-

prehensive, uniformly treated material, of individuals who in childhood had been affected by pylorospasm, seem likely to produce a definite answer to the question of a connection between pyloric hypertrophies in infants and adults, respectively.

### Summary.

After a description of the symptomatology and the patho-anatomic basis of pyloric hypertrophy in infants and in adults, the question is discussed whether there is any genetic connection between the two forms of disease. In the opinion of the author, no such connection exists. In the light of two cases of old caustic injuries in the stomach, the part, if any, played by the chronic gastritis with regard to the occurrence of pyloric hypertrophy in the adult is investigated. The conclusion is drawn that the chronic gastritis constitutes that pathogenetically active factor in the pyloric hypertrophy of the adult.

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## **“Ligamentous” Ankle Fractures.**

### **Diagnosis and Treatment.**

By

NIELS LAUGE-HANSEN.

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In “Ankelbrud I” (Dissertation, 1942, NIELS LAUGE-HANSEN) it is described how the manner of production (genesis), pathological anatomy, characteristic roentgenogram (genetic roentgen diagnosis), and technique of reduction (genetic reduction and maintenance) of the ankle fractures met with in clinical work were established by means of combined experimental-surgical and experimental-radiographical investigations. There are 4 types of ankle fractures which patho-anatomically occur in constant and characteristic stages.

The types of ankle fracture are characterized by the localization and form of the fibular fracture, and the stages within each individual type are determined according to the combination of the fibular fracture with other fractures involving the ankle region.

When type and stage have been determined, the pathological anatomy is given, also with regard to which ligamentous ruptures may be present in the different types of ankle fracture (see “Ankelbrud I”, pp. 307—320).

It is emphasized that detachment of medial or lateral ligaments of the ankle is often an equivalent to a fracture of the medial or lateral malleolus.

In all the 4 types of ankle fracture, stage I is, or may be, a ligamentous detachment, *i. e.*, a “ligamentous” ankle fracture.

In the literature it is often still deplored that sprain and ligamentous rupture involving the ankle region are dark points, and

that these affections often cause diagnostic and therapeutical difficulties and result in disability.

In order, if possible, to find the underlying cause of this trouble a material consisting of all ambulant and hospitalized patients who were referred to roentgen examination in the Central Hospital, Randers, during the twelvemonth from July 1, 1947, to June 30, 1948, for fresh lesion of the ankle region was made the object of a closer investigation.

If there is a lesion at stage I, and this lesion is a ligamentous detachment, it is not by far always possible to demonstrate it by ordinary roentgen studies; but nevertheless it is easy to obtain a precise and exact diagnosis by a special roentgen examination. Its efficiency will appear from the material. In the following each individual type of ankle fracture will be dealt with, particularly the varieties with ligamentous detachments only.

*Supination-Adduction Fracture I, i. e.*, transverse fracture in a varying height of the lateral malleolus or rupture or detachment of ligamentum calcaneo-fibulare and ligamentum talo-fibulare posterius. Detachment occurs at the attachments of these ligaments (see Figs. 1—2), either at the tip of the lateral malleolus or on the calcaneus and talus.

These ligamentous detachments are demonstrable in an ordinary roentgenogram only when a bone shell large enough to be visible on the film has been torn off. If this is not the case, and a ligamentous fracture is suspected, a special roentgen examination must be made in the frontal plane, while the hind foot is adducted. The distal part of the crus is fixed with one hand while the other grasps around the foot at the calcaneus from the plantar aspect and moves it medially — adduction. This is done with a vigorous and persistent adduction pull and may be accomplished without anesthesia. In this way a distinct varus position of the talus in the "malleolar fork" (tibio-fibular mortise) occurs, and the distance between the talus and the tip of the lateral malleolus is increased, indicating ligamentous detachment laterally (Figs. 3—4).

By roentgen examination under ordinary supination of the foot, which is sometimes recommended, the varus position of the talus in the malleolar fork will not occur unless the supination is very vigorous, and a simultaneous inversion (inward rotation) of the foot is carried out, by which the hind foot is adducted to a certain extent. This manoeuvre will cause a strong muscular fixation



and intense pain owing to tightening of the tendons running behind and distal to the lateral malleolus. If the hind foot is adducted as described in the preceding paragraph, it is possible to avoid these troubles which may to a smaller or greater extent disturb the roentgen examination and lead to an erroneous result. Considering that ligamentous detachment takes place along the entire lateral surface of the talus, and that there is often a simultaneous rupture of the joint capsule of the posterior talo-calcaneal articulation strengthened with a ligament laterally (see Fig. 1), it will be realized that the affection is a serious lesion.

The lesion is very frequent, but so far it is rarely diagnosed primarily, as there is no or only faintly visible changes of the bones in the roentgenogram, and as roentgenograms taken under adduction are not commonly used. We have often experienced that the lesion is not diagnosed primarily. Such a case is shown in Figs. 5—8. Note the changes of the posterior talo-calcaneal articulation, which may account for the difficulties experienced by the patients. That it is so will be seen from the material which the author intends to review a little later on.

*Supination-Eversion Fracture I, i. e.,* detachment of ligamentum malleoli lateralis anterior, is not roentgenologically demonstrable when it occurs as an isolated lesion, except when a shell of bone large enough to be seen in the lateral view has been torn off, but this is generally not the case. By a special roentgen examination it is sometimes possible to demonstrate its presence by means of fourth projection, but it may also be diagnosed clinically (when the roentgen examination has shown no sign of ankle fracture) by the presence of a swelling corresponding to the ligament and a very distinct tenderness corresponding to the ligamentous attachment on tuberculum anterior tibiae and on the proximal part of the anterior margin of the lateral malleolus.

*Pronation-Abduction Fracture I, i. e.,* fracture of the medial malleolus or detachment of the deltoid ligament. If the ligament has been detached with a shell of bone not large enough to be demonstrated roentgenographically, nothing abnormal will be seen in the roentgenogram of the ankle region since the talus generally occupies its normal position in the malleolar fork. By a special exposure in the frontal plane under abduction of the hind foot (the distal part of the crus is fixed, and the calcaneous part of the foot is grasped and moved laterally), the talus will adopt a valgus position in the "malleolar fork", and the articular space between

Ligamentum malleoli lateralis anterior.

Ligamentum talo-fibulare anterior.

Ligamentum calcaneo-fibulare.

Ligamentum talo-calcaneum.



Fig. 1. Specimen of the lateral aspect of the ankle joint. Note attachments of ligaments!

LAUGE HANSEN. "Ligamentous" Ankle Fractures.



Ligamentum talo-fibulare posterius.

Ligamentum talo-fibulare anterius.

Malleolus lateralis.

Fig. 2. Specimen of the lateral aspect of the ankle joint after production of supination-adduction-fracture I with transverse fracture through approximately the middle of the lateral malleolus (Note attachments of ligaments!).

LAUGE-HANSEN. "Ligamentous" Ankle Fractures.



Fig. 3. Ligamentous detachment laterally with the talus in varus position under adduction of the hind foot.



Fig. 4. Roentgenogram of the same ankle joint without adduction.

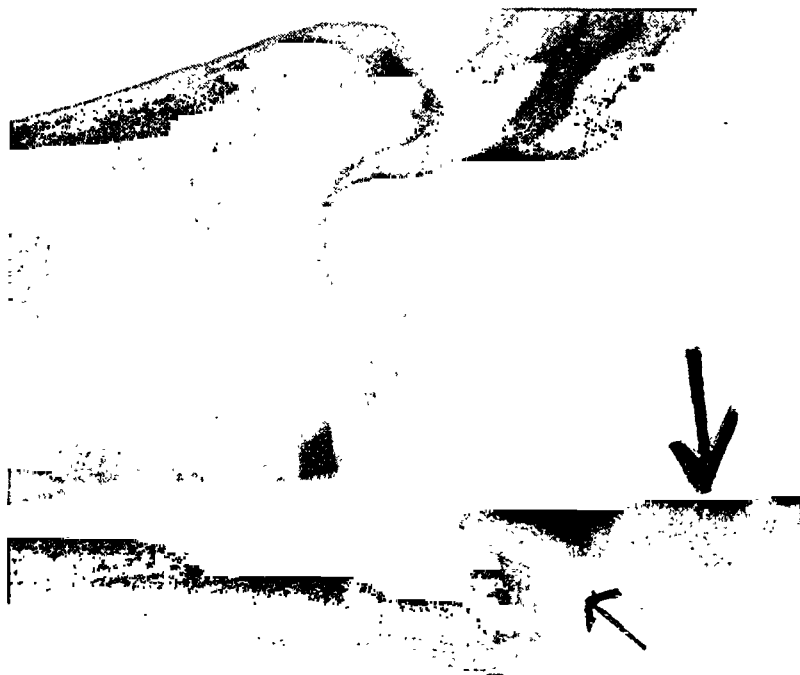


Fig. 5.

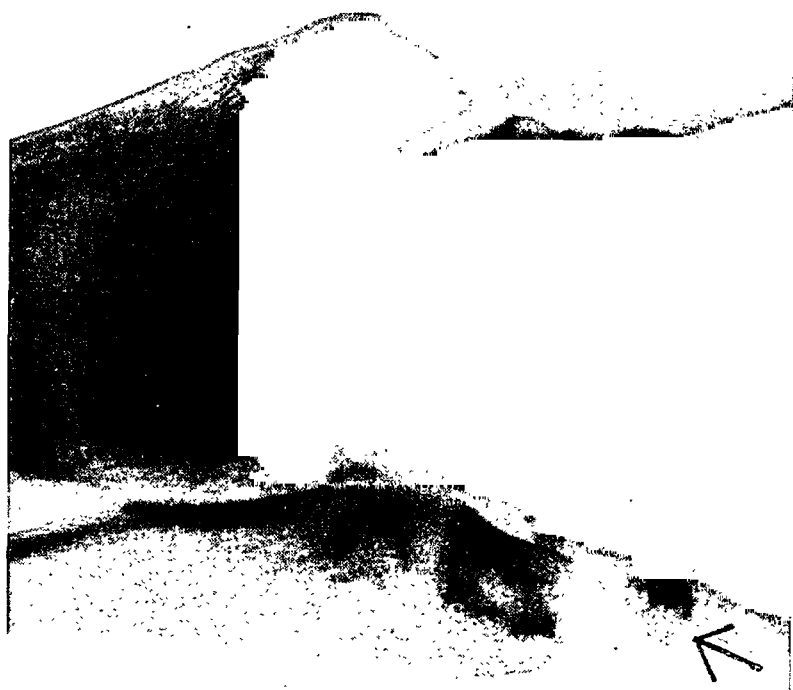


Fig. 6.

Figs. 5 and 6. Two year old and untreated case of supination-adduction-fracture I (ligamentous).

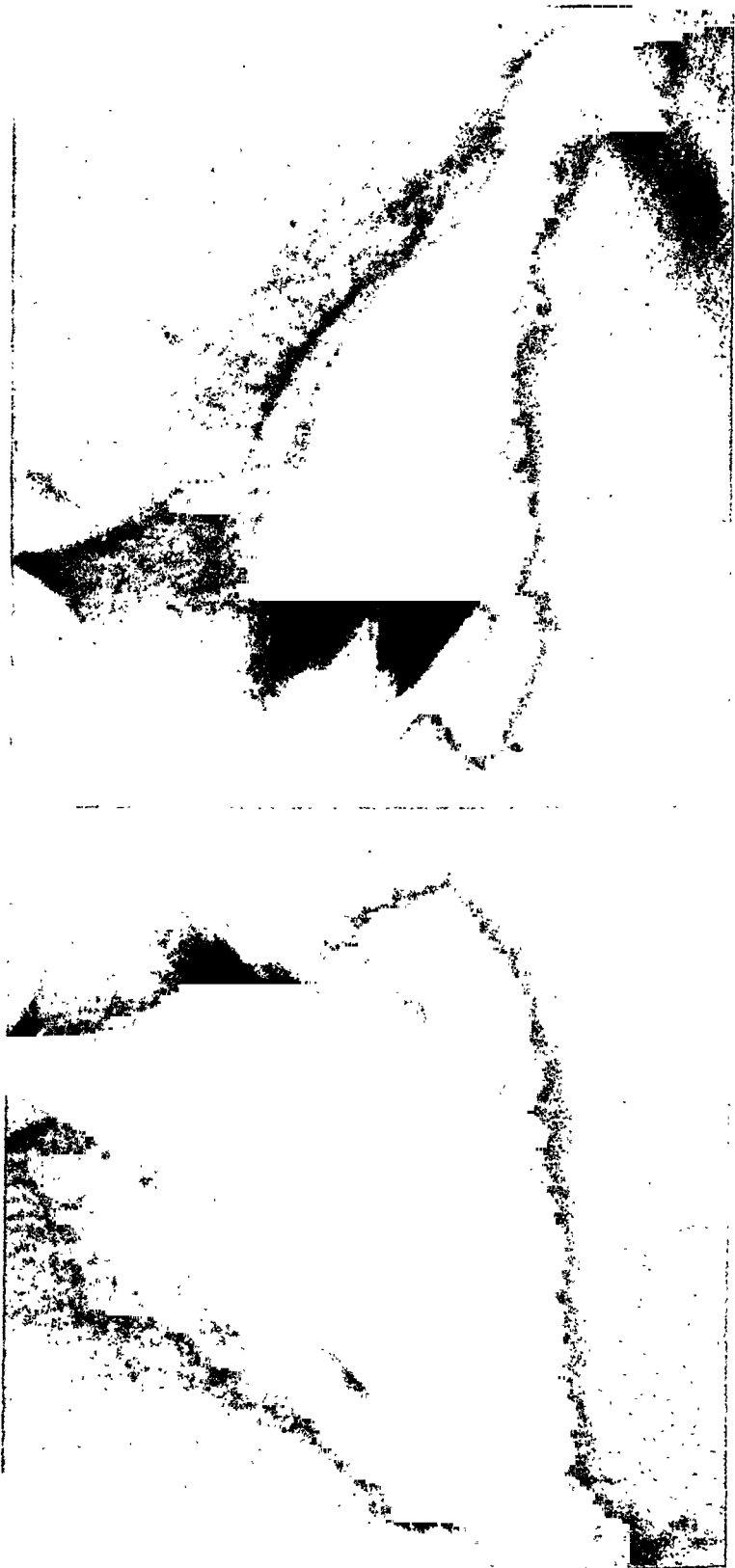


Fig. 7.  
Figs. 7—8. Same case, X-ray the changes of the posterior talo-calcaneal articulation (Fig. 7).



Fig. 9. Ligamentous detachment medially with increased width of the articular space between the medial malleolus and talus under abduction of the hind foot.



Fig. 10. Roentgenogram of the same ankle joint without abduction.

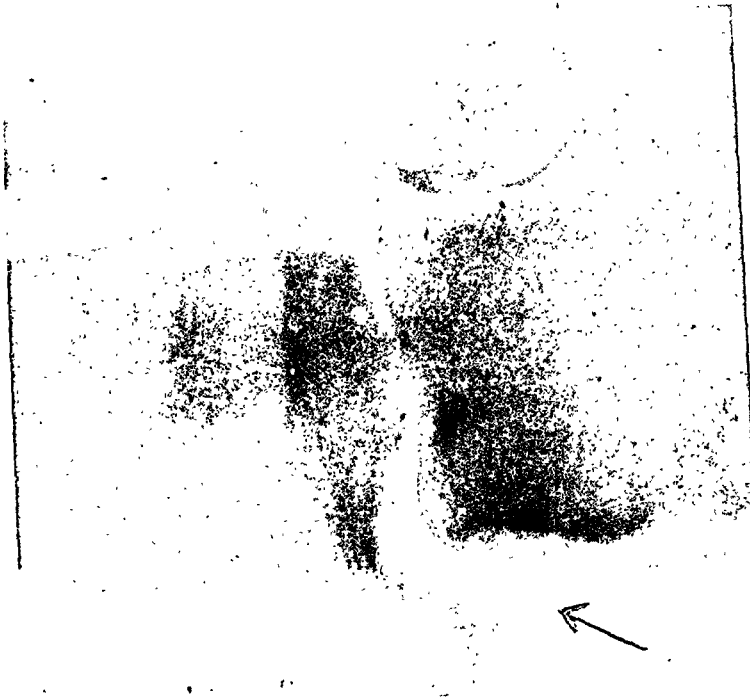


Fig. 11. Ligamentous detachment medially and in the syndesmosis (ligamenta malleoli lateralis anterior et interosseum) with increased width of the syndesmotie space and the articular space between the medial malleolus and talus, the latter being in valgus position due to eversion (outward rotation) of the foot.

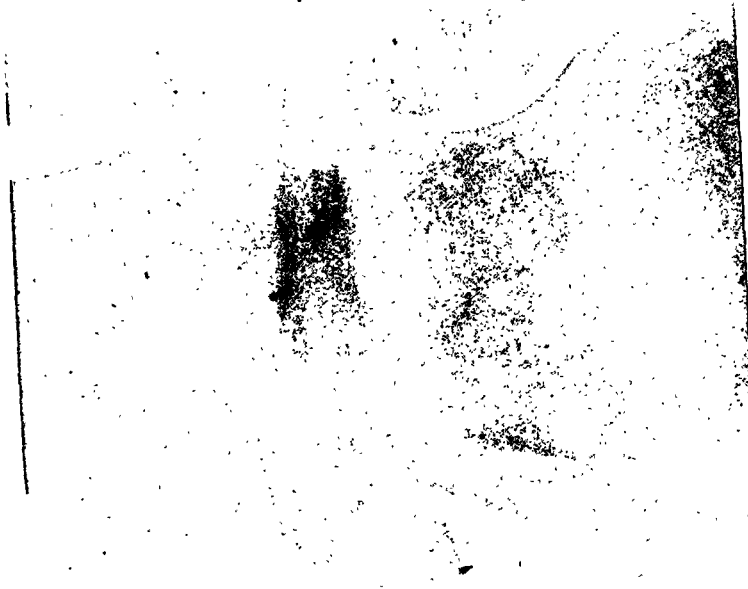


Fig. 12. Roentgenogram of the same ankle joint without eversion.



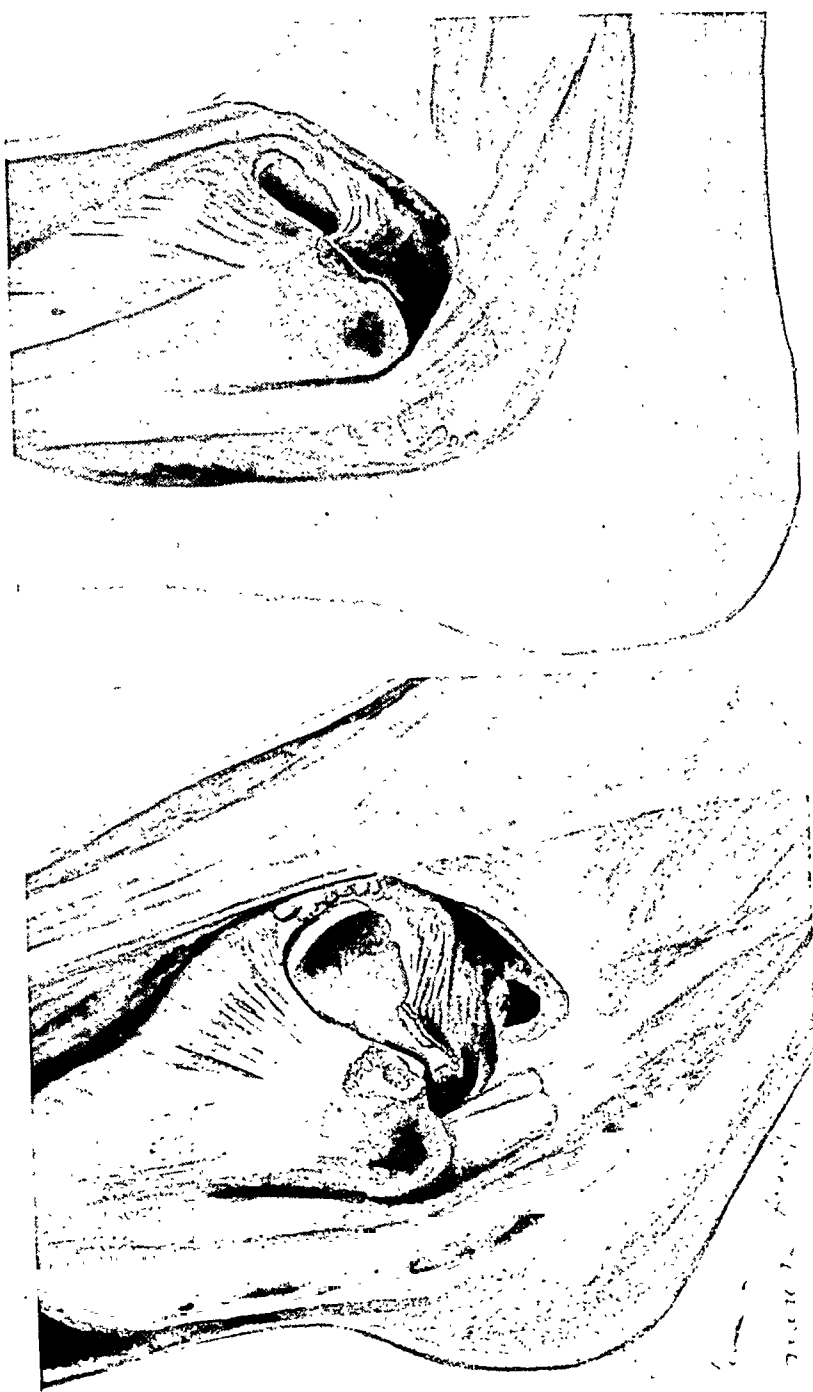


Fig. 13 b.

Fig. 13 a.

Figs. 13 a, b & 14. Drawings of supination-inversion lesion I and II (detachment of ligamenta talo-fibulare anterius (I) et calcaneo-euboidum (II)).

Fig. 13 b shows the result of reduction — the foot pronated and dorsiflexed.

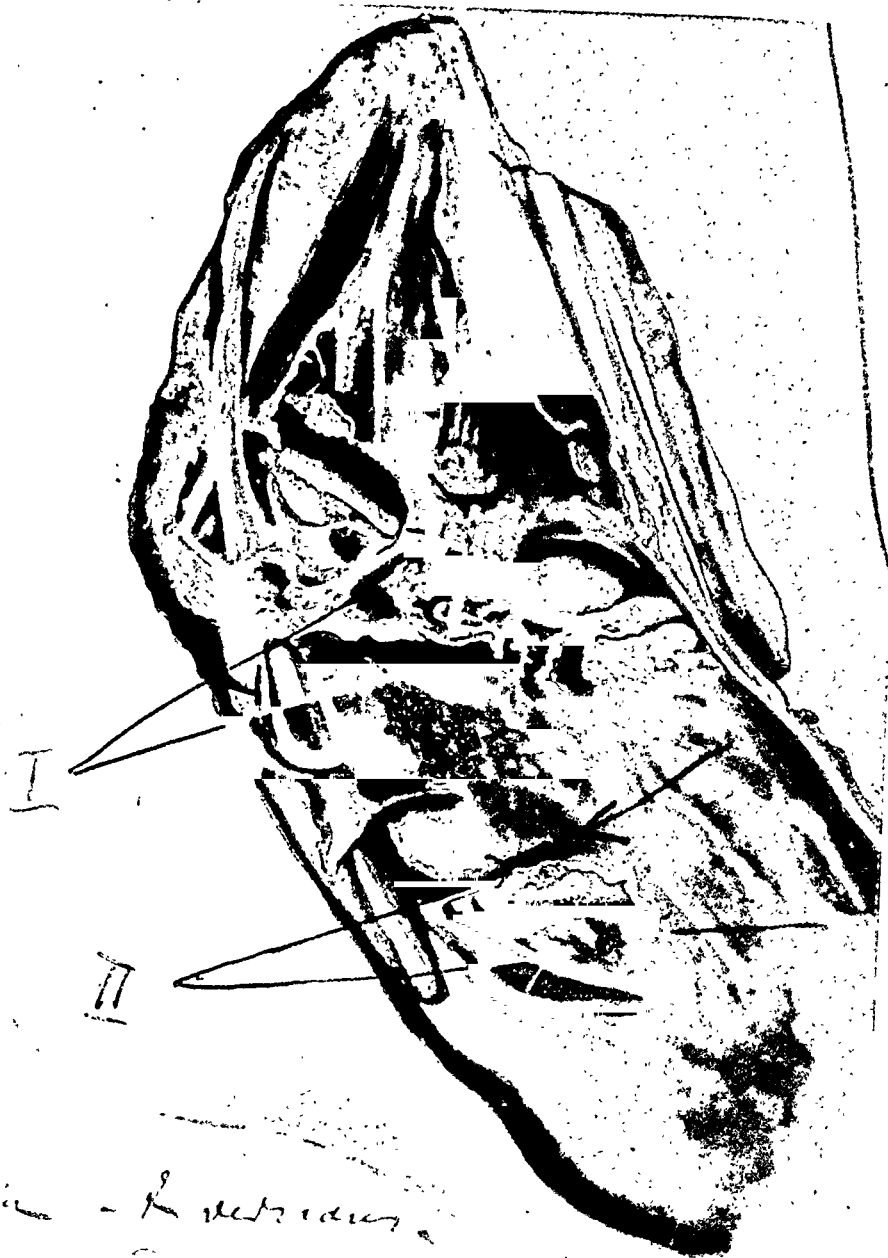


Fig. 14.

LAUGE-HANSEN. "Ligamentous" Ankle Fractures.



Fig. 15 a.



Fig. 15 b.

Fig. 15 a, b. Two clinical cases with small fragments at the calcaneo-cuboid articulation (supination-inversion lesion stage II).

the medial malleolus and talus is widened, indicating a ligamentous lesion (Figs. 9—10).

*Pronation-Eversion Fracture II*, i. e., lesion as in pronation-abduction fracture I (which see) + detachment of ligamentum malleoli lateralis and ligamentum interosseum tibio-fibulare. (Strictly speaking it ought to be designated as stage I, since stage I of pronation-eversion fracture corresponds to pronation-abduction fracture I, and since it is actually stage II (the lesion of the ligaments of the syndesmosis) which denotes and is the commencement of the pronation-eversion type of fracture.) If in this type there is no fracture of the medial malleolus, but detachment of the deltoid ligament, it will generally be impossible to demonstrate it roentgenologically as the position of the talus in the malleolar fork is completely normal, and the syndesmotie space presents natural conditions. If, on the other hand, a roentgenogram is taken in the frontal plane while the foot is everted (rotated outward), it will be possible to demonstrate valgus position of the talus in the "malleolar fork", increase of width of the interspace between the talus and medial malleolus, and of the syndesmotie space (Figs. 11—12).

In the following table the ratio of incidence of the 4 types of ankle fracture of the material from 1942 will be found.

For the purpose of comparison the ratio of incidence of the types of fracture of the material from July 1, 1947, to June 30, 1948, is also cited in the table.

Supination-Adduction Fracture	1948	1942
Stage I (ligamentous) .....	19	
Stage I .....	10	25
Stage II .....	9	23
	38 = 35.8 %	48 = 15.5 %
Supination-Eversion Fracture		
Stage I .....	4	8
Stage II .....	14	72
Stage III .....	7	48
Stage IV .....	10	84
	35 = 33 %	212 = 68.6 %
Pronation-Abduction Fracture		
Stage I (ligamentous) .....	5	
Stage I .....	4	6
Stage II .....	4	9
Stage III .....	5	3
	18 = 17 %	18 = 6 %

Pronation-Eversion Fracture	1948	1942
Stage II (ligamentous) .....	7	
Stage II .....	2	4
Stage III .....	4	4
Stage IV .....	2	18
	<hr/> 15 = 14 %	<hr/> 26 = 8.3 %

The material from 1942 originates from Copenhagen, *i. e.*, a purely urban population.

The material from 1948 is, as already mentioned, from Randers, and a considerable portion of the patients belongs to the rural population.

In an urban population the ratio of incidence of supination-eversion fractures is larger than in a rural population, which accounts for some of the difference in the ratio of incidence of the two materials.

But the most essential part of the difference is, however, due to the large number of "ligamentous" ankle fractures which were demonstrated in the material from 1948. The number of these fracture (31) is relatively large, particularly in the supination-adduction group, but it is also considerable in the pronation-abduction and pronation-eversion groups.

Thus the investigations presented here seem to show that if a special roentgen examination is omitted in case of the presence of clinical symptoms of lesion of the ankle-joint region, *approximately 30 % of serious lesions, i. e., the "ligamentous" ankle fractures, will not be diagnosed primarily.*

In addition to these ligamentous lesions, all of which can be included in the genetic classification of ankle fractures, since they are equivalents to malleolar fractures and have the same genesis, there is another ligamentous lesion in the ankle region, which is also very frequent.

This lesion is detachment or rupture of ligamentum talo-fibulare anterius (see Fig. 13 a and b).

This lesion is produced by a vigorous inversion (inward rotation) of the maximally supinated foot. By experimental-surgical investigations, the results of which have been presented at a meeting of the Danish Society of Surgeons (Nordisk Medicin, Bd. 32, p. 2337, 1946) the author succeeded in producing this lesion experimentally. It is rarely roentgenologically demonstrable. When the possibility of ankle fracture has been ruled out by roentgen examination, it may be diagnosed clinically by the

presence of a (generally considerable) swelling corresponding to the localization and surroundings of the ligament laterally on the dorsum pedis, and a very distinct tenderness corresponding to the attachment of the ligament on the *distal* part of the anterior margin of the lateral malleolus and on the lateral surface of the collum tali. A secondary lesion in this mechanism of fracture may be rupture of the ligament strengthening the lateral and plantar aspects of the calcaneo-cuboid articulation (Fig. 14). A dorso-plantar roentgenogram of the mid foot can give the diagnosis by showing grain-sized osseous avulsions from the lateral contour of the cuboid and calcaneus, and thus affords a diagnosis not only of the second lesion (Fig. 15 a, b), but also indirectly of the first.

As far as the treatment of these lesions is concerned, the readers are referred to the conclusion of AAGE BERNTSEN's article: "On Arthrodesis Talo-Cruralis in Painful Sequelae of Malleolar Fractures" (U. f. L., p. 82, 1944). It says, "In order to prevent the occurrence of these disabling conditions anatomical reduction according to NIELS LAUGE-HANSEN's technique should be employed . . .".

As isolated lesions of ankle ligaments are equivalents to ankle fractures with regard to genesis, tendency of dislocation, and mechanism of genetic reduction and maintenance, the reduction and maintenance of position of the reduced fractures should be as in case of ankle fractures.

In supination-eversion I and supination-inversion I immobilization (with the foot pronated and dorsiflexed) for 3 weeks will suffice.

Supination-adduction I, pronation-abduction I, and pronation-eversion II require longer immobilization. Generally a period of 10—12 weeks is recommended, but in the author's experience 6 weeks will presumably suffice in most cases, provided that the injury is diagnosed at once, and the fracture is reduced and immobilized in a plaster cast in conformity with the genesis.

### Summary.

Among 106 lesions of the ankle joint, submitted to X-ray examination during a year in the X-ray department of the central hospital, Randers, 31 "ligamentous" ankle fractures were found.

These are not visible on ordinary roentgenograms, but are only to be demonstrated by a special technique which is described. The "ligamentous" ankle fractures are serious lesions which are classified just like ordinary ankle fractures, and have to be treated in the same way by reduction and immobilization in plaster of Paris. Further is described a common "ligamentous" lesion of the ankle, not included in the usual types of ankle fracture. It is produced by forced inversion (inward rotation) of the supinated foot.

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## Surgical Aspects of the Adrenaline-Content in Blood.

By

SVANTE ANNERSTEN.

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### 1. Method.

The important questions involving the reactions of the vascular system on surgical operations are probably unanswerable unless the variations of adrenaline in the blood are taken into account. This lacuna in our knowledge about a fundamental domain is chiefly due to the difficulty of exactly determining the adrenaline content in the blood by reasonably simple methods in the laboratory.

The methods of determining adrenaline are in principle of two different kinds, biological and chemical. The former is very complicated and therefore impossible in clinical practice.

In principle the chemical methods are based on an oxidization of the adrenaline.

KOBRO (1946), attempted to determine the blood adrenaline photometrically by arsenic-molybdenum after precipitation with trichloroacetic acid. His values were approximately 0.05  $\mu\text{g.}$  per ml. blood. The most specific and sensitive method in use today is the one based on a fluorescence phenomenon described by GADDUM and SCHILD in 1934 (but discovered as early as 1930 by PAGET). This fluorescence is caused by subjecting adrenaline in alkaline solution to irradiation by ultraviolet light. The most persistent difficulty in connection with this method has been the troublesome "eigen-fluorescence" of other substances in the plasma, chiefly proteins. HUEBER (1940), KALAJA and SAVOLAINEN (1941), JÖRGENSEN (1945) and WEST (1947) have tried to combat this difficulty by dialyzing the blood. These authors thus get an adrenaline concentration of 0.04—0.10  $\mu\text{g.}$  per ml. blood.



LEHMANN and MICHAELIS (1942) adopted another method. They filtered away the extraneous fluorescence (= the "eigen-fluorescence" of plasma which is blue while that of adrenaline is green) by *optical* means. This enabled them to measure the specific fluorescence of adrenaline. The light intensity, is, however, so insignificant that it is difficult to measure in a photometer. Thus, VON PORAT (1946) was unable to measure "normal

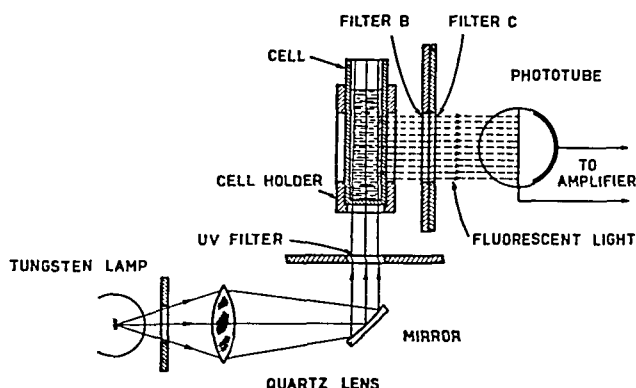


Fig. 1. Diagram of fluorescence measurement in spectrophotometer.

values" of the adrenaline content in blood. Using Pulfrich's photometer the author for a long time attempted in vain to obtain reproducible results. Only after I had, in collaboration with GRÖNWALL and KÖIW, adopted Beckmann's spectrophotometer with a fluorescence accessory-set (and in other respects a modification of LEHMANN's and MICHAELIS' method) did I obtain certain figures with respect to the adrenaline content in plasma. The outstanding advantage of Beckmann's spectrophotometer is its great sensitivity in conjunction with the objective registration with a photoelectric cell which, in addition, makes possible very rapid readings. This latter factor is of particular importance as the fluorescence of adrenaline attains its maximum in  $\frac{1}{2}$ —3 minutes (depending on alkalinity and other circumstances) and then rapidly fades away. Our "normal values" agree quite well with those found by LEHMANN and MICHAELIS: 1—3  $\mu$  gr. adrenaline per ml. plasma.

In principle the analysis is carried out as follows: 4 ml. of blood are drawn from the cubital vein and transferred with 2 ml. buffer solution (citrate-thiosulphate) to a pyrex centrifuge tube. Adrenaline in this solution is stable for at least 24 hours. After 15 minutes of centrifuging 1 ml. of plasma is transferred to a cuvette of corex glass. 2 ml. of 10 percent NaOH solution are added. After stirring with a pyrex glass rod

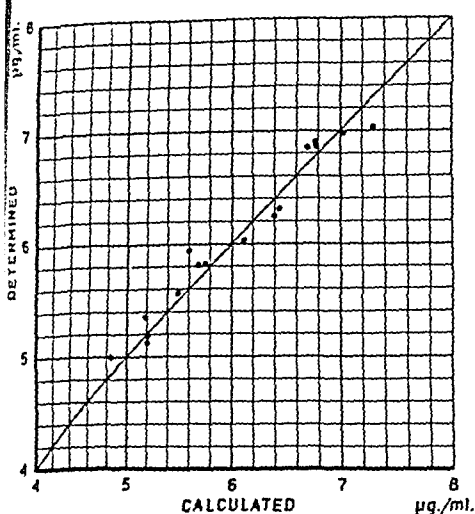


Fig. 2. Adrenaline values in additive experiments.

Each point = one determination.

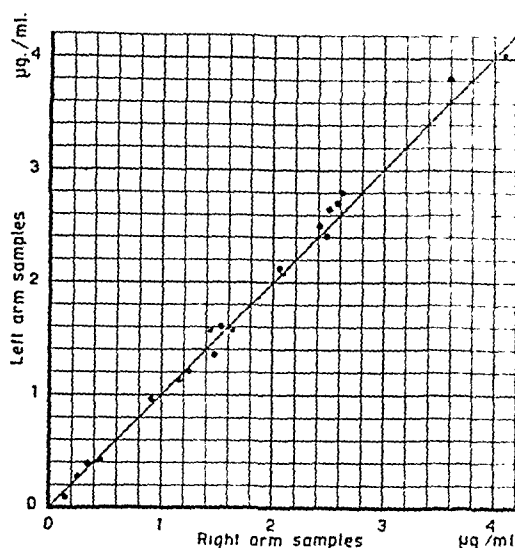


Fig. 3. Adrenaline values in blood from right and left arm.

Specimens from the same person taken simultaneously.

(an important detail!) the cuvette is placed in the spectrophotometer. The principle for measuring the fluorescence herein is illustrated in fig. 1.

The fluorescent light is filtered through an optical system which lets through the green light of adrenaline only and this affects the photoelectric cell which in its turn governs a galvanometer. The maximum reading is taken, as a rule after  $1\frac{1}{2}$  minutes (= reading A). Now 0.1 ml. of 40 percent formaline solution is added. This entirely neutralizes the fluorescence specific to adrenaline. The remaining fluorescence represents the "eigen-fluorescence" of plasma. After approximately 5 minutes this has reached its minimum which is read off (= reading B). Then 0.1 ml. of 0.005 percent freshly prepared adrenaline solution is added. After stirring the reading at maximum fluorescence is noted. This occurs already after 10 seconds or thereabouts (= reading C).

The formula  $\frac{A - B}{C - B} \times K$  gives the quantity of adrenaline per ml. expressed in micrograms. K is a predetermined factor calculated from a solution of known adrenaline concentration.

The addition of a known quantity of adrenaline to plasma of known adrenaline concentration demonstrates good agreement between calculated and obtained adrenaline concentrations. (Fig. 2.)

The error of method is insignificant ( $n = 16$ ,  $\sigma = 0.1$ ). This is shown in fig. 3 where specimens taken at the same time from the right and the left arm have been registered.

There is no reason to doubt that the values obtained really represent adrenaline. None of the several authors who have put

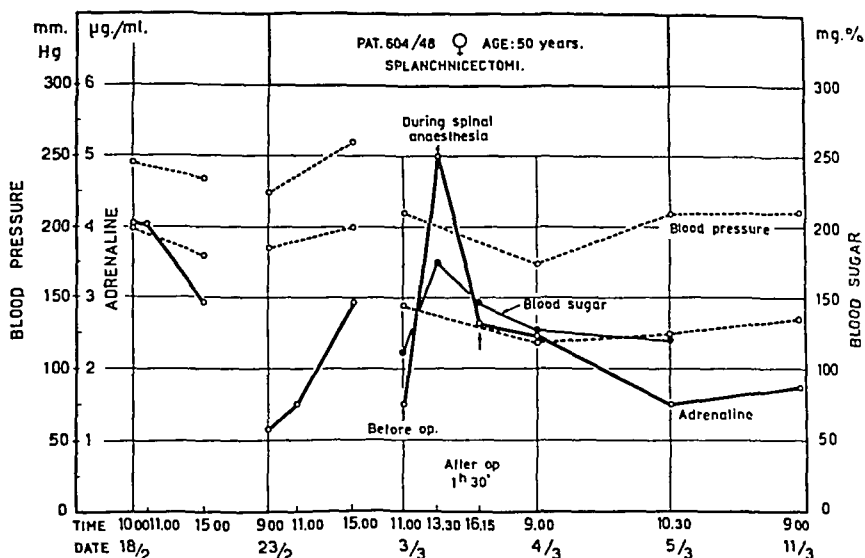


Fig. 4. Hypertonia cases. Adrenaline and blood pressure for 2 days before operation. Adrenaline, blood pressure and blood sugar during operation and for some days thereafter.

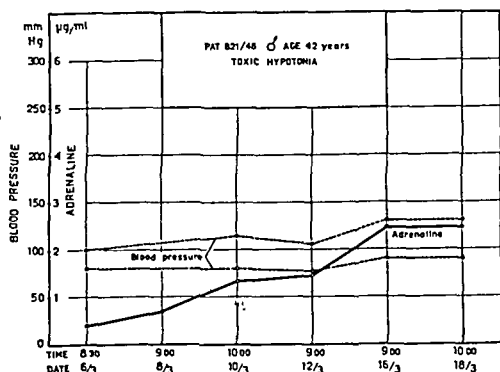


Fig. 5. Case of hypotonia with spontaneous improvement. Adrenaline and blood pressure determined every other day.

the Gaddum-Schild fluorescence method to the test have found anything to contradict its adrenaline specificity. Not even nor-adrenaline reacts identically. A large number of substances contained in plasma have been tested by, among others, JÖRGENSEN and LEHMANN and MICHAELIS, for example, acetone, acetylcholine, aneurin, ascorbic acid, cortin, creatinin, ethyl alcohol, fatty acids, glucose, lactic acid, glycogen, glycolcoll, heparin, histamin, insulin, phosphoric acid, several salts, tyrosin to take an example. In my own studies I have found that bilirubin does not disturb the fluorescence, but, according to LEHMANN and MICHAELIS gall

salts and iron and copper salts to a certain extent impair the intensity of the fluorescence.

In two cases, where hyper- and hypotonia respectively were relieved spontaneously or by operation, I have found a remarkable parallelism between changes in blood adrenaline and blood pressure (figs. 4 and 5). Similarly in an animal-experiment with shock (see fig. 8).

In most operative cases and in animal experiments there is, as will be discussed in a subsequent section, a certain parallelism between blood sugar and blood adrenaline. This is highly compatible with the fact that adrenaline increases blood sugar. LEHMANN and MICHAELIS have demonstrated that in rats the fluorescence disappears completely 5 hours after an adrenalectomy. JÖRGENSEN found a very insignificant fluorescence remaining in dialyzed blood from adrenalectomized rabbits.

## 2. The Nature of Blood Adrenaline.

Comparisons between our determinations on plasma and plasma dialyzate are of the greatest interest. Table 1 gives the adrenaline content of dialyzed plasma as being only 2—3 per cent of the total adrenaline content. The figures for the dialyzates agree quite closely with those found by *e. g.* JÖRGENSEN and WEST. They are also of the same magnitude as some figures determined by biological means. FALTA and IVCOVIC (1919) considered that some of the adrenaline in blood was bound to an-

Table I.

Exp. No.	Adrenaline in plasma before dialysis	$\mu$ g 1/ml Adrenaline in plasma after 4 hours dialysis		% adrena- line in dialysate
		in impermate	in dialysate	
1.....	1.83	1.70	0.050	2.7 %
2.....	3.30	2.70	0.082	2.7
3.....	1.17	1.13	0.031	2.7
4.....	1.51	1.42	0.040	2.7
5.....	1.89	1.84	0.051	2.7
6.....	2.38	2.24	0.065	2.7
7.....	3.19	2.91	0.081	2.5
8.....	1.80	1.62	0.054	3.0
9.....	1.52	1.48	0.046	3.1
10.....	1.68	1.64	0.046	2.7

other substance. LEHMANN and MICHAELIS reason along the same lines. The investigations made by the author prove that the incomparably greater part of the blood adrenaline is bound to some non-dialyzable substance, probably protein since the blood adrenaline disappears after treatment with protein precipitants (e. g. chloracetic acid).

The quantity of "free" adrenaline is insignificant and difficult to determine. The action of adrenaline is extremely rapid, and the fleeting "maxima" of adrenaline may be impossible to catch by biological methods or chemical dialytic methods, unless continuous registration is arranged for. However, as will be shown in the following, the author has found considerable increases in the adrenaline contents in various clinical states. This implies that *the blood adrenaline is probably not broken down as rapidly as was hitherto supposed, but is almost immediately bound and therefore will be biologically inactive*. By chemical methods it is then possible to determine whether there has been an adrenaline excess. The increases in the adrenaline content of the blood being very large, and with reference to the powerful effect of much smaller quantities of free adrenaline injected intravenously, this mechanism must imply much greater certainty than a slower breaking-down process would afford. That, however, the adrenaline breaks down relatively rapidly in the blood is shown by the clinical investigations to be described where not only rapid increases but also rapid decreases in the adrenaline contents occur.

### 3. Clinical Investigations.

#### A. Normal Values and Sources of Error.

LEHMANN and MICHAELIS, whose procedure we have adopted in principle, found in 42 normal test persons a mean value of 1.87  $\mu$ g. adrenaline per ml. of blood; the minimum value was 1.00 and the maximum value 3.16. In dialyzed blood from 35 persons JÖRGENSEN found a mean of 0.068  $\mu$ g. adrenaline per ml., minimum 0.041 and maximum 0.096.

In 10 normal cases the author found a mean of 2.6  $\mu$ g. adrenaline per ml. (min. 1.00, max. 4.1) in blood specimens taken 8—9 o'clock in the morning. In 7 of these cases specimens were also taken at 13 hours and at 15 hours. The daily variations were small (mostly in cases of recumbent fracture patients) but a slight

Table II.

*µg/ml adrenaline in blood specimens at various times of day  
(Normal cases).*

No.	8—9 A. M.	13 p. m.	15 p. m.
1.....	1.00	1.06	1.28
2.....	1.22	1.54	1.35
3.....	1.70	1.80	1.36
4.....	3.80	2.75	2.75
5.....	4.10	3.90	3.95
6.....	2.80	2.95	2.04
7.....	2.50	2.00	1.00

tendency to decrease later in the day was observed. This is shown in *table II.*

If this group is also allowed to include the operative cases where specimens were taken at 8 o'clock in the morning before the operation, the total number of cases will be 27. *Then the mean value for the adrenaline content will be 2.33 µg. per ml.*

In estimating the importance of the blood adrenaline concentration we must chiefly consider the psychical factors. Psychological excitation increases the adrenaline secretion of the suprarenal glands. In animal experiments CANNON estimated the adrenaline increase to 3.2—3.7 µg. per kg. per minute in states of excitement. LEHMANN and MICHAELIS teased a dog. The concentration of adrenaline in the venous blood immediately increased from 1.38 µg. to 2.34 µg., after 3 minutes the concentration was 1.89 µg. and after 20 minutes 1.70 µg. Using a biological method OKAMURA could prove that in states of excitement in man the blood adrenaline increased 5—10 times.

Naturally in dealing with operative cases where specimens are taken before, during and after the incision, it is necessary to take into account psychical affectations in the form of anxiety and pains. The individually conditioned irritability probably plays an important part, possibly also age and sex.

LEHMANN and MICHAELIS have demonstrated that bodily exertions often involve a slight reduction in the concentration of blood adrenaline. This is also a circumstance to be reckoned with in the postoperative period when pains may cause protracted muscular contractions.

Save the above we know practically nothing of how the surgical diseases here discussed per se affect the adrenaline concentration

in the blood. In the knowledge of the author only KALAJA and SAVOLAINEN and JÖRGENSEN have touched upon these problems without, however, being able to draw any certain conclusions.

In estimating the significance of the changes in the concentration of blood adrenaline caused by various surgical operations we must, therefore, reckon with considerable sources of error through factors which have nothing to do with the operation as such. These "extra-surgical" factors do, on the other hand, contribute to our knowledge of the changes occurring in the body when an operation is being carried out.

Another matter which still more complicates the proper interpretation of the adrenaline changes is the extreme rapidity with which adrenaline is secreted into the blood and again disappears from it. How quickly these reactions actually take place is not properly known, but according to the above mentioned experiment by LEHMANN and MICHAELIS on a dog a slight increase in the adrenaline content could still be demonstrated after 20 minutes. It is almost certain that we here are dealing with bound adrenaline. (Cf. Chapter 2.) Although a series of tests only in exceptional cases hits the real adrenaline maxima, there should be some possibility of following the concentration changes of the total adrenaline. *A raised adrenaline value tells us that an increased secretion of adrenaline has taken place.*

### **B. The Blood Adrenaline Content before, during and after Operations.**

Together with NORINDER the author (1946) demonstrated that most major operations despite being normal were followed by an excess of sugar in the blood. The behaviour of the blood pressure pointed to the probability of a certain vasoconstriction, and, therefore, that an adreno-sympathetic stimulation was, as in the case of initial shock, caused by operations, especially in the abdomen. The present investigation therefore pays special attention to concentration of adrenaline and sugar in the blood in such operations.

In a total number of 22 operative cases the blood adrenaline and blood sugar contents were determined at the same time. As a rule the blood specimens for both these analyses were taken simultaneously — in the morning before the operation, when complete anaesthesia had set in and 1—2 hours after the finished operation, also on the morning of the day after the operation and two days after it. Figs. 6 and 7 illustrate four typical curves ob-

Table III.

Pat.			Op.	Anaes- thesia	μg adren/ml (left) mgm% blood sugar (right)									
No.	Age	Sex			Morning		After anaest.		1—2 hours after op.		1 day after op.		2 days after op.	
1366	59	M.	Ventr. resect.	Spinal	2.5	210	1.9	165	1.4	245	0.6	140	—	—
682	43	M.	»	»	2.4	120	3.6	180	4.6	160	1.0	145	1.4	125
367	59	M.	»	»	2.0	125	0.5	—	3.3	180	2.7	190	1.7	—
1000	25	M.	»	»	2.3	135	1.6	130	3.2	250	1.8	160	1.5	140
933	71	M.	»	Splanch.	1.1	100	1.5	105	0.9	200	2.1	125	1.2	120
1309	52	M.	»	»	1.5	150	1.0	220	0.2	165	0.9	245	0.6	230
659	44	M.	Chole- cystect.	Spinal	4.0	125	1.3	200	3.7	260	1.9	160	1.4	135
672	50	W.	»	»	2.8	150	3.7	145	3.0	145	1.5	105	—	—
721	49	M.	»	»	4.0	120	0.1	190	0.7	260	2.2	125	3.3	120
277	75	M.	»	Splanch.	—	100	4.7	—	—	—	9.6	230	5.7	140
342	61	W.	»	»	3.9	150	5.7	—	1.9	125	2.5	180	2.2	170
1375	69	M.	»	Spinal	1.0	95	0.8	230	1.0	160	0.7	175	1.4	200
368	64	M.	Prostat- ectomy	»	4.3	115	4.8	240	2.6	180	2.9	125	4.4	130
336	65	M.	»	»	2.7	—	—	180	4.8	280	1.7	150	2.0	90
368	64	M.	»	Sacral	4.2	110	4.8	240	2.6	180	3.6	125	4.4	130
397	30	M.	Thoraco- plastic	Narcot.	1.4	130	5.6	—	3.7	235	7.8	205	1.5	150
556	29	M.	»	»	1.3	120	2.4	200	0.7	185	1.9	140	2.0	110
458	65	M.	Column- fix.	Spinal	1.4	110	2.8	155	2.1	130	1.2	125	—	—
1170	20	M.	Strumect.	Local	1.1	115	1.5	140	1.6	130	1.8	140	0.7	110
1397	50	M.	»	»	2.1	170	—	—	2.0	130	—	—	0.9	150
1396	78	M.	Anus praeter.	Spinal	2.3	115	0.1	195	0.2	190	0.3	55	(Diabetes)	
604	47	W.	Splanchnect.	»	1.5	110	5.0	170	2.6	150	2.5	130	1.5	120

tained from such figures. Table III gives a graphic representation of all the cases.

Owing to the above mentioned sources of error the values obtained are difficult to interpret. With the increasing effect on blood sugar of adrenaline in view a certain parallelism between the adrenaline and blood sugar curves could have been expected. A reasonably pronounced parallelism can, however, be demonstrated in only half (11) of the operative cases. That the remaining 11 cases give no evidence of parallelism in this respect need, however, not exclude the possibility that the hyperglycemia, which occurs in practically all the cases, is due to an increase in adrenaline. The time interval between the specimens is so long that a destruction of adrenaline may have set in. It is natural to suppose that an excess of adrenaline is followed by a pause in adrenaline secretion and that a blood specimen taken at such



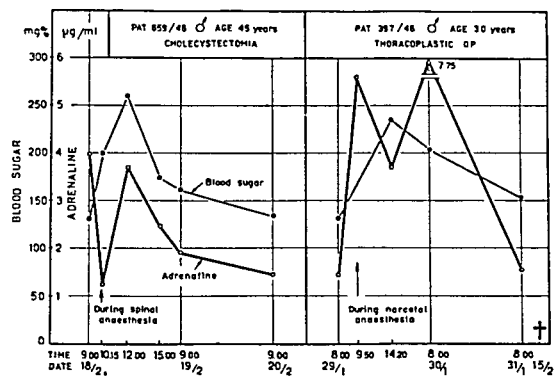


Fig. 6. 2 operations.

Thoracoplastic case choked. Fatal outcome after few days.

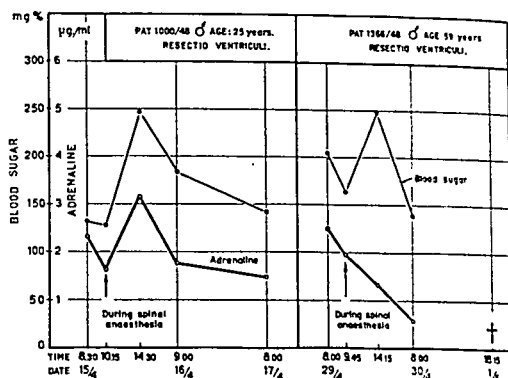


Fig. 7. 2 operations.

The second case died in pneumonia.

times gives low values. On the other hand, the adrenaline does not mobilize the liver glycogen quite instantaneously. Several authors (*e. g.* GEIL 1943, and WARMING-LARSEN, 1947) have demonstrated that intravenously injected adrenaline results in a significant increase in the blood sugar only after  $\frac{1}{2}$  hour and maximum increase after  $1\frac{1}{2}$  hours approximately. After that the blood sugar concentration returns to the initial value at approximately the same rate. These authors have also proved that the blood sugar increase is dependent on the functional health of the liver — hepatitis results in less hyperglycemia on the administration of adrenaline. With these circumstances in view it is more remarkable than not that the adrenaline and blood sugar curves are synchronized in as many as 50 per cent of the cases.

Even the preparations for an operation, including the anaesthetizing, often result in a hyperglycemia, which becomes more pronounced immediately after the operation but later tends to subside and which almost certainly depends on an increase in the adrenaline content in the blood. Owing to the fact that the adrenaline is bound to other substances, the author's method in some cases affords a means of demonstrating this increase. The investigations indicate that the major operations in question (mainly ventricular resections, cholecystectomies, prostatectomies, thoracoplastic operations and strumectomies) very frequently give rise to adreno-sympathetic compensatory states of excitation such as in early shock, to be supervised and rapidly treated as such — with adequate liquid therapy and not with so called stimulants.

As we see in Table III the types of anaesthesia adopted in abdominal operations in this material were spinal anaesthesia ac-

according to Seebrecht and posterior splanchnic anaesthesia according to Kappis. 7 of the 10 spinal anaesthesias show a clearly reduced blood adrenaline content when complete anaesthesia set in. In 2 of these cases there were scarcely any traces of adrenaline. This is what could be expected since the visceral reflexes and thereby an important phase of the mechanism acting on the adreno-sympathetic system no longer function. The falling blood pressure is a sign of this. To keep this under control in the usual manner 1—2 ml. of Sympatol was administered subcutaneously in most cases. (The author is at present studying how Sympatol influences the adrenaline and blood sugar levels.)

In 3 of the spinal anaesthesia cases the adrenaline content increased already before the operation. One case was a splanchnicectomy to relieve hypertonia, the other two abdominal operations (ventricular resection and cholecystectomy respectively). In all these cases the blood pressure was reduced, the reduction being stopped with Sympatol. The adrenaline tests were taken when the blood pressure was on the increase.

In 4 cases of splanchnic anaesthesia there was an increase in blood adrenaline even before the operation in 2 cases, a reduction in 2. In 3 cases, however, the differences were insignificant. This form of anaesthesia is consequently less disturbing to the adreno-sympathetic system.

Of both the cases of thoracoplasty (in Narcotal narcosis) one showed fairly small blood adrenaline variations and a fleeting, moderate hyperglycemia. This case healed without complications. The other case, on the other hand, which, having double-sided TBC-disorders, had an unfavourable prognosis and died after 4 days. The patient was shocked and received blood transfusions in connection with and after the operation. Here both blood adrenaline and blood sugar were much increased (fig. 7), a fact pointing to the probable importance of the adrenaline increase in shock.

Two more fatal cases occurred in this series of operations. One was a 78-years-old diabetic with inextirpable cancer recti who died following the operative formation of an artificial anus. The operation (under spinal anaesthesia) exhibited a decreased adrenaline concentration which remained post-operatively. The section showed bronchopneumonia and parenchymatous organic degeneration. The other case died of a fulminant pneumonia on the second day after ventricular resection. Here also the postoperative

course showed an uninterrupted decrease in the concentration of adrenaline (fig. 6). The section evidenced bilateral pneumonia and pronounced degeneration of the parenchymatous organs. It seems probable that the parenchymatous degeneration and bad circulation had a deleterious effect on the adrenaline secretion of the suprarenal glands. This shows that *in septic conditions and in the later stages of shock it is possible to find evidence of impaired adrenaline function* and the importance of using vascular stimulants in such cases.

The 3 prostatectomies yielded no significant increases in adrenaline concentration. It is remarkable, however, that 2 of the cases had high preoperative adrenaline values which decreased postoperatively but returned to the initial values after 2 days. They are old persons who have difficulty in mobilizing their adrenaline. The most vital of these old people did, however, react with fairly marked adrenaline and blood sugar increases 2 hours after the operation.

It is surprising that the two cases of Basedow's disease, where relatively high adrenaline values could be expected before, during and after the strumectomy, evidence low values with small variations and no really significant increase in either blood adrenaline or blood sugar. A few other thyreotoxicoses were studied already prior to the start of iodine treatments. Even then the blood adrenaline values were low.

An investigation into the influence of age on the blood adrenaline concentration shows no significant difference between the normal values of old and young persons. Patients over 60 years of age did, however, exhibit a tendency to react with a smaller increase in adrenaline in connection with operations than persons less old. The material is still too small to allow certain conclusions to be drawn. The same applies to any sexually conditioned differences. It is, however, striking that all the 3 women already in the anaesthesia stage, preoperatively, manifested increased blood adrenaline concentrations. Is this perhaps a manifestation of greater psychical irritability?

### C. Summary of the Clinical Investigations.

Despite the fact that clinical series determinations of blood adrenaline encounters great difficulties, chiefly owing to the strong psychical dependency of the adrenaline secretion and also because the adrenaline is rapidly eliminated from the blood, the

investigations exhibit manifestly significant variations in the blood adrenaline content in operated persons in contradistinction to non-operated persons.

Of 22 operated cases 11 exhibited increased blood adrenaline concentrations 1—2 hours after the operation. Even 24 hours later 7 cases manifested slightly higher values than before the operation, in some cases, however, not more than the normal variation for the 24-hour period. 2 days after the operation the adrenaline concentration is in all cases slightly lower than or approximately the same as before the operation. In all cases save 1 the blood sugar is increased by the operation, an increase which is still significant the day after the operation but thereafter decreases. In 11 of the cases there was a certain parallelism between the adrenaline and blood sugar curves. It is therefore *probably that the adrenaline increase causes the hyperglycemia and that the operation must be looked upon as an initial stage of shock.*

In 7 of the 10 spinal anaesthesias the adrenaline concentration falls during the anaesthesia. In splanchnic anaesthesia and local anaesthesia and narcotal narcosis there is as a rule a slight increase in the blood adrenaline content already before the start of the operation.

Both the cases of strumectomy studied exhibit low adrenaline values both pre- and postoperatively. These values are changed but little by operation.

Three cases of death occurred shortly after the operation. One case (thoracoplasty) exhibited shock and very large adrenaline increases. The 2 others (abdominal operations) during and after the operation manifested incessantly falling adrenaline values. Both went ad mortem in pneumonia and toxic suprarenal insufficiency is probable.

#### 4. Animal Experiments.

Two animal experiments have so far been carried out with adoption of the method to be described.

The Arteria carotis of a Numal-anaesthetized and heparinized cat was connected to a manometer for pressure registration on a chymograph. Blood specimens were taken from vena jugularis for adrenaline and blood sugar determination. After laparotomy, shock was induced by manipulation of the intestines. Immediately after these manipulations a brief increase in blood pressure was

noted (fig. 8). The blood adrenaline and blood sugar increases were registered at the same time. Then the blood pressure fell while the shock continued. Repeated specimens taken after 8 and 17 minutes respectively exhibited decreasing adrenaline and blood

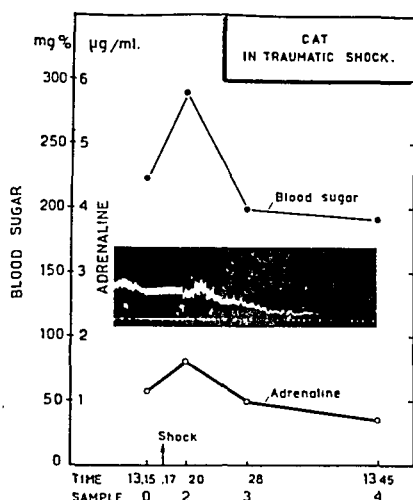


Fig. 8. Blood pressure, blood adrenaline and blood sugar curves in cat during visceral shock.

sugar values. The last blood sample was drawn immediately before the animal died. The rapid course of events is probably due to a combination of traumatic and hemorrhagic shock (owing to the heparin visceral hemorrhages were quite considerable).

The most noteworthy finding from this experiment is the striking parallelism between blood adrenaline, blood pressure and blood sugar. That in this case the initial traumatic shock involved adrenaline increase, vasoconstriction and hyperglycemia is beyond every doubt. Vasoconstriction and hyperglycemia in shock have long been recognized and an adrenaline increase has therefore been considered probable. This experiment would seem to prove that such is the case.

The rapid fall in blood sugar is surprising. We have however, also encountered this phenomenon in the clinical operative cases. Several authors (*e. g.* WARMING-LARSEN, SUNABA, ASADA) have demonstrated that injections of adrenaline bring the blood sugar to a maximum after approximately 1 hour, and that the induced hyperglycemia persists for a few hours. Possibly the adrenaline excess induced by a state of shock differs somehow from an ordinary solitary adrenaline injection. The former may possibly cause more widespread hormonal reactions, particularly in the

pancreas, with more rapid glucose breaking-down. In experiments on narcosis JÖRGENSEN obtained similar rapid variations in the blood sugar content.

It is also surprising that the blood-adrenaline concentration

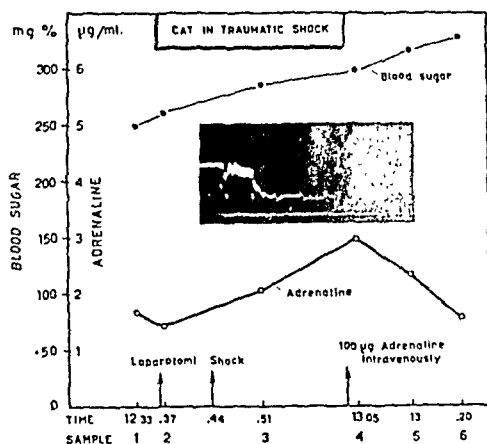


Fig. 9. Blood pressure, blood adrenaline and blood sugar curves in cat before and during shock. Intravenous adrenaline injection towards end of shock. Adrenaline increase transient but blood sugar continues to increase owing to adrenaline injection.

falls in the final stages of shock. In these cases the developing oligemia probably reduces the activity of the suprarenal glands. A similar decrease in blood adrenaline was exhibited by two of the above mentioned cases of postoperative death. Also in an other shock experiment on cat (fig. 9) the adrenaline content increased in the initial stages of the shock despite the yielding blood pressure owing to continued hemorrhage. This increase is therefore of compensatory nature. The blood sugar continued to increase. After intravenous injection of adrenaline a very brief rise in adrenaline concentration was noted together with the increased blood pressure. Then the adrenaline content fell rapidly but the blood sugar level continued to rise owing to the injection of adrenaline.

Previously there has been a tendency to overestimate the deleterious rôle played by the adrenaline increase in shock. In early shock the adrenaline increase is adequate since it maintains an otherwise sinking blood pressure. Inordinately accentuated vasoconstriction does, however, impair circulation and makes the oligemic condition worse. The investigations of the author do, however, indicate that in *advanced* shock of traumatic or toxic nature the secretion of adrenaline is also reduced in a catastrophic manner.

## Summary.

1. A partly new and improved method for determining the adrenaline content in blood is described. The method, developed by the author in collaboration with GRÖNWALL and KÖRW, is based on measurements of the fluorescence of adrenaline and is a refinement of the method of LEHMANN and MICHAELIS.

2. The blood adrenaline is present both in free and bound form, probably to protein. Dialytic experiments have proved that the dialyzable adrenaline fraction merely amounts to 2—3 per cent of the total adrenaline.

3. Under various circumstances the blood adrenaline concentration may increase considerably. Since such large quantities of adrenaline in biologically active form are probably not tolerated by the system, this "surplus" adrenaline is rapidly converted to an inactive form prior to somewhat slower destruction. Owing to this process the author's method, determining total adrenaline, can actually have time to show the changes in the blood-adrenaline concentration. In all probability this method is the best one in use at present for clinical purposes.

4. The adrenaline concentration in venous blood from 27 persons was determined to approximately 2.3  $\mu$ g. per ml. plasma (max. 4.1, min. 1.0) in morning specimens. Daily variations were rather insignificant.

5. Tests on patients before, during and after operations (ventricular resections, cholecystectomies, thoracoplastic operations, prostatectomies, and strumectomies) yielded, in approximately half the cases, a postoperative increase in the blood adrenaline concentration. In some cases the increase set in during the anaesthesia, before the operation. In practically all the operative cases the blood-sugar level increased postoperatively. This is a probable consequence of the adrenaline excess. In approximately half the cases there was a clear parallelism between the blood adrenaline and blood sugar curves. Major operations always seem to induce a stage of initial shock.

6. Thyreotoxicoses exhibit low adrenaline values with insignificant variations both pre- and post operatively.

7. Of 10 cases of spinal anaesthesia 7 exhibited falling adrenaline values when anaesthesia was complete, a consequence of the extinction of the visceral sensations and reduced splanchnic stimulation of the suprarenal glands.

8. One operative case with a tendency to shock manifested very considerable adrenaline increases. Two cases who died in pneumonia exhibited an uninterrupted reduction of the adrenaline content of the blood. This is interpreted as a manifestation of toxic suprarenal insufficiency.

9. Visceral-traumatic shock was experimentally induced in cats. Here the author found clear parallelism between blood sugar, blood pressure and blood adrenaline in the form of initial increase and terminal decrease.

10. Factors like psychical irritation, muscular exertion and the rapidity with which even the total adrenaline is broken down strongly influence the blood adrenaline concentration and render difficult its determination, especially in clinical material.

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## Curare in the Treatment of Tetanus.

By

ERNST TRIER MØRCH.

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As early as 1859 WELLS tried the effect of curare in the treatment of tetanus, but it was not until CLAUDE BERNARD's pioneer investigations in 1865 that curare came into extensive use. It was mainly used in France and Germany for the treatment of a number of widely different conditions for which there was no known remedy, *e. g.* epilepsy, chorea, hydrophobia, and strychnine poisoning (HOFFMANN 1879, PETZOLD 1882, DOMINE 1894, HOCH 1894, BINZ 1895, CHESTERFIELD 1904, GERGELL & LEVY 1904, LAWEN 1906).

All attempts failed, however, to produce the desired action because the preparations were too impure and heterogeneous. Crude curare contains a number of different, very active alkaloids, notably curine, which has a slight curare-like action, but also has a toxic effect on the heart and causes a fall in blood pressure.

The active alkaloids were not purified before about 1935 (KING) after which time curare came into general use throughout the world. Its use in tetanus, however, was mainly confined to desperate cases, and the results were rather disappointing (COLE 1935, MITCHELL 1935, WEST 1936, CULLEN & QUINN 1943, HANNA 1946).

In normal subjects curare paralyses all striated muscles, but in tetanus its effect is not the same. Even when given in large doses it affects mainly the convulsions, while the normal muscle function remains unaffected, unless massive doses are given. It is therefore possible to relieve the convulsions while the respiration remains normal or only slightly affected.

The action of curare is brief. This is an advantage for its use in anaesthesia for the treatment of fractures and dislocations, etc., and in psychiatric shock treatment, but it is a disadvantage in the treatment of neurological disorders and tetanus, where a more prolonged action is required. The effect of subcutaneous and intramuscular injections, whether in aqueous solution or oily suspension, is difficult to control; while during continuous intravenous administration shock with haemoconcentration may occur. The cause of the latter is unknown; it may be (1) a direct action of the curare on the blood vessels, which become permeable to proteins, (2) a histamine effect, since curare can liberate histamine in certain circumstances, or (3) a result of the poor circulation caused by the prolonged muscular relaxation.

The best method of administering the curare is by intermittent intravenous injections, in quantities sufficient to control the convulsions, but at intervals sufficiently long for the muscles to regain their normal tone now and again and perhaps to begin to show faint signs of tetanus. There is great variation in the dose and interval required in different cases.

Curare has no anodyne or sedative effect, and therefore hypnotics, *e. g.* morphine, and sedatives, *e. g.* avertin or barbiturates, or both (MOVIN), may be administered at the same time. Sedatives reduce the spasms and relieve the patient of much suffering and should be used according to the methods already accepted, but they probably do not improve the prognosis (PERDRUP). It is not known whether curare is an exception to this rule, but its use, by checking the convulsions, allows time for the tetanic intoxication to subside.

The immediate cause of death in tetanus is usually either pneumonia or shock, and the patient's condition must be studied several times a day. Records must be kept of the temperature, pulse rate, blood pressure, haemoglobin %, erythrocyte sedimentation rate, serum protein, chloride, and bicarbonate content, blood urea, and daily output and specific gravity of the urine, so that the treatment can be modified according to the findings. Probably the fluid intake should be restricted, since the patient is lying still and there is a tendency to hypostasis.

*Pneumonia* should be prevented by penicillin. The use of sulphur drugs is not recommended as the daily output of urine is low. The maintenance of a clear airway and administration of oxygen are often neglected. In several respects the condition re-

sembles that of prolonged poisoning from sleeping drugs seen in suicide cases, most of whom also die of pneumonia. These deaths can nearly always be prevented by frequent energetic bronchoscopic aspirations and administration of oxygen.

For the maintenance of a clear airway, a bronchoscope, a laryngoscope, and tracheal catheters must be at hand (and also a staff trained in their use). There are, of course, risks in the use of these instruments, but they are outweighed by the advantages. A respirator must also always be available all the time, as sudden respiratory embarrassment due partly to the condition itself and partly to the curare and other drugs, is common. The modern treatment of tetanus must be carried out in close collaboration with an experienced anaesthetist.

*Case Report.* A male, aged 25, developed tetanus following a burn. His condition is described in detail by PERDRUP.

*Report of the Treatment:* The temperature was raised, but fell immediately after the bronchoscopic aspiration. It may be that the raised temperature in these cases is usually pulmonary in origin. It appears that we should have repeated the bronchoscopic aspiration on June 6th at 12 midday (temperature 38.9 C), but this was not done as there were no abnormal sounds on auscultation. The spasm effect of bronchoscopy must be disregarded as it is counteracted by the anaesthetic and by more curare. The atelectasis found in the right upper lobe at postmortem examination could probably have been avoided by more frequent aspiration.

The blood pressure remained satisfactory until shortly before death.

The figures for *haemoglobin and serum protein* suggest that the patient ought perhaps to have received more blood. The only estimation made of the *serum chloride and bicarbonate* showed normal figures.

The *daily output of urine* was low throughout, but the patient sweated a great deal. The *specific gravity of the urine* was high, but the method of determining it was very inaccurate. It may be that we allowed the patient too much fluid (pulmonary oedema) or perhaps he should have had the same amount of fluid (the blood urea was 50 mgm. per 100 cc. on June 6th), but with a higher content of substances with big molecules, *e. g.* protein, blood or glucose.

*Sedatives and morphine* were given in small amounts, but the patient did not have much pain, because of the curare.

*Magnesium sulphate and curare* are probably a good combination, as the magnesium sulphate prolongs the action of the curare.

The curare used was first "Tubocuran" (Alfred Benzon), and then "Tubarine" (Burroughs Wellcome). Both preparations contain 10 mgm. of d-tubocurarine-hydrochloride per ml. and there was no demonstrable difference between the effects of the two preparations. At first glance the dose may seem very big, but it was never too big. It was obvious that the curare eased the patient's distress so that he did not suffer.

Date	Hour	May		June	June 5							June 6				June 5 + 6				
		26	28	4	15	16	17	18	19	20	22	23	24	Total	3-5	6-9	9-12	12-15	15-17	Total
Examinations.	Temperature (centigrade) .....	39.6	39.6	37.7	38.6				39.4	38.8			Bronchosc. aspirat.		37.0	38.9				
	Pulse rate .....	106	106	78					116	100			95		100	120				
	Blood pressure .....					100									140		110	70		
	Haemoglobin (siccæ) .....	100				85			78		78		5.3		80	84	6.9			
	Serum protein % .....	6.8	5.3		4.9												310			
	» chloride																			
	» bicarbonate, millimol. .															34				
Daily output of urine.	Daily output of urine, ml. ....	800	1,150					50		50				100		350			350	450
	Specific gravity of urine .....	1,022	1,021					1,027		1,025						1,030				
Administration of fluid.	Oral ml. ....			3,800	1,500									1,500					0	1,500
	Intravenous: saline, ml. ....																		1,500	1,500
	glucose, gm. ....													80			1,500 ml.		40	120
	dried serum (1 portion = 500 ml.) .....																			
	blood .....								1,500						1,500	500	500		500	2,000
Medication.	Luminal, cg. ....																			
	Narcodorm <sup>1</sup> , g, rectally .....											1							0	1 gm.
	Magnesium sulphate, g., intramusc. ....			15	10														0	10 "
	Morphine, cg, subcut. ....																			
	Curare, mg, intraven. ....																			
	» mg., intramusc. ....																			
									10	20	10	10	5	15	25	95	10	20	15	15
												</								

The details of the treatment which might have been better are given in the table.

1. Probably too much fluid or insufficient diuretics were given.
2. Too little blood was given.
3. The aspiration from the bronchi should probably have been more energetic.

### Conclusion.

Curare treatment is still in the experimental stage, but it should be used as it has big advantages.

Curare treatment requires a highly qualified staff who are used to working together.

Curare treatment requires considerable equipment.

The curare treatment of tetanus should probably be centralized.

### Summary.

A brief review of the literature and of the effect of curare is given. The case of a man aged 25, who developed tetanus after a burn is discussed. The case is reported by A. PERDRUP in this number of *Acta*. The patient was treated with curare (Tubarine, and a similar Danish preparation "Tubocuran"). He received a total dose of 170 mgm. intravenously, and 90 mgm. intramuscularly in 24 hours. This was just sufficient to control the convulsions. Glucose, dried serum and whole blood were also given, and bronchoscopic aspirations were performed.

The patient died. It is possible that he was given too much fluid and too little blood, and bronchoscopic aspiration should probably have been carried out more frequently. The dosage of curare was satisfactory.

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